R&D Day 2019

Update on Research Programs

February 28, 2019

Nasdaq: ALDX

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Agenda

• Opening Welcome	Todd Brady, CEO
• Corporate Strategy & Pipeline Growth	David McMullin, CCO
• Proliferative Vitreoretinopathy – A Rare Retinal Disease	Dean Eliott, M.D. Harvard Medical School Mass. Eye and Ear Infirmary
• Ocular Disease Area Program Updates	David Clark, CMO
• Ocular Disease Area Market Opportunities	Chris Pearson, VP Commercial
• Conclusion	Todd Brady, CEO
• Q&A	

Our Mission

Developing Next-Generation Medicines to Improve the Lives of Patients with Immune-Mediated Diseases

~7%

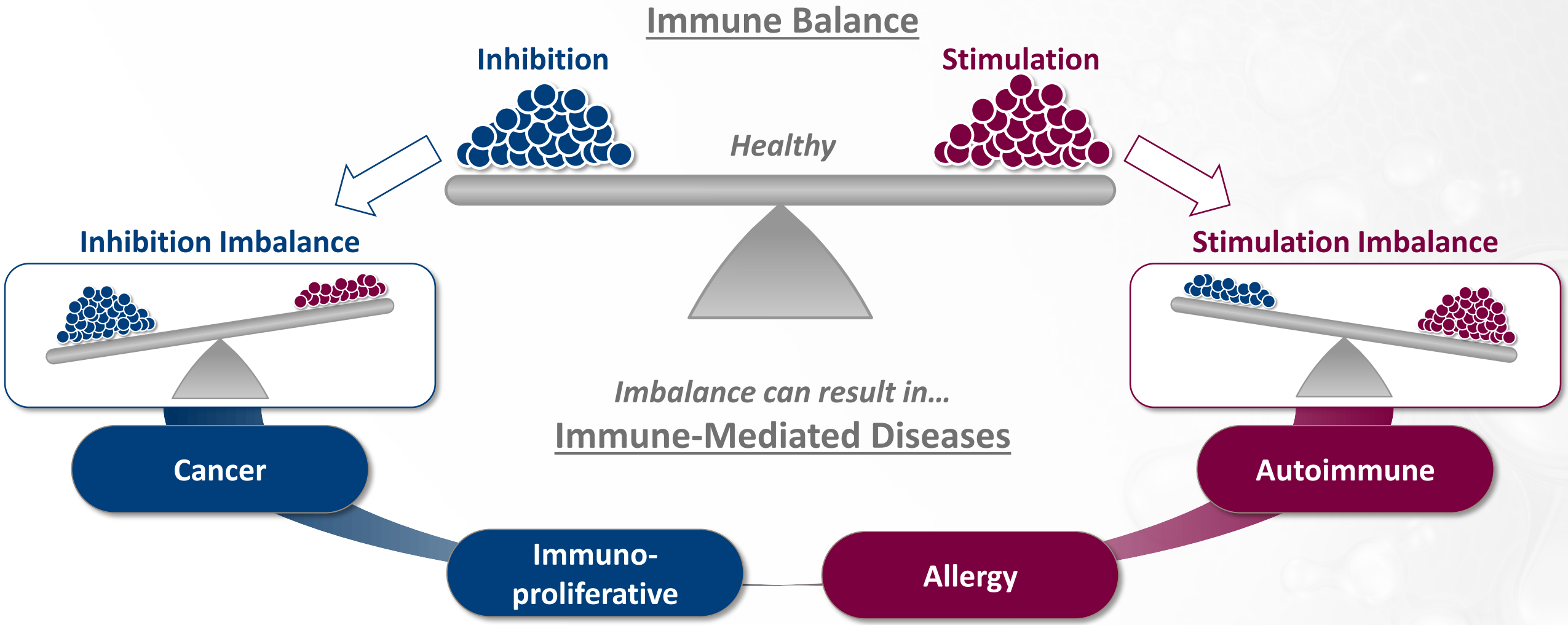
Of Western Society

Suffer from some form of **immune-mediated disease**, and **incidence is increasing**

Disease control elusive despite existing therapies, and thus **novel approaches are needed**

Source: Lerner, Jeremias, and Matthias, International Journal of Celiac Disease, vol. 3, no. 4 (2015): 151-155;
Shurin and Smolkin, Advances in Experimental Medicines and Biology 601:3-12, 2007; Kuek et al, Postgraduate Medical Journal 83(978): 251-260, 2007.

Immune System Imbalance Leads to Immune-Mediated Disease



Deliberate Focus on Ocular Diseases and Select Systemic Diseases

ALDEYRA THERAPEUTICS™

2004	…	May 2014	2015	2016	2017	2018	2019
Founded		IPO; First Phase 2 IND filing	First Phase 2 Initiations	First Phase 2 Completions	First Phase 3 Initiations	Add'l Phase 2; Add'l Phase 3	Potential First Phase 3 Completions*

DOMAIN ASSOCIATES

Johnson & Johnson INNOVATION

Discovery & Preclinical

Ocular Diseases

- RASP Dry Eye Disease
- RASP Allergic Conjunctivitis
- RASP Noninfectious Anterior Uveitis
- DHFR PVR
- RASP Retinal Disease

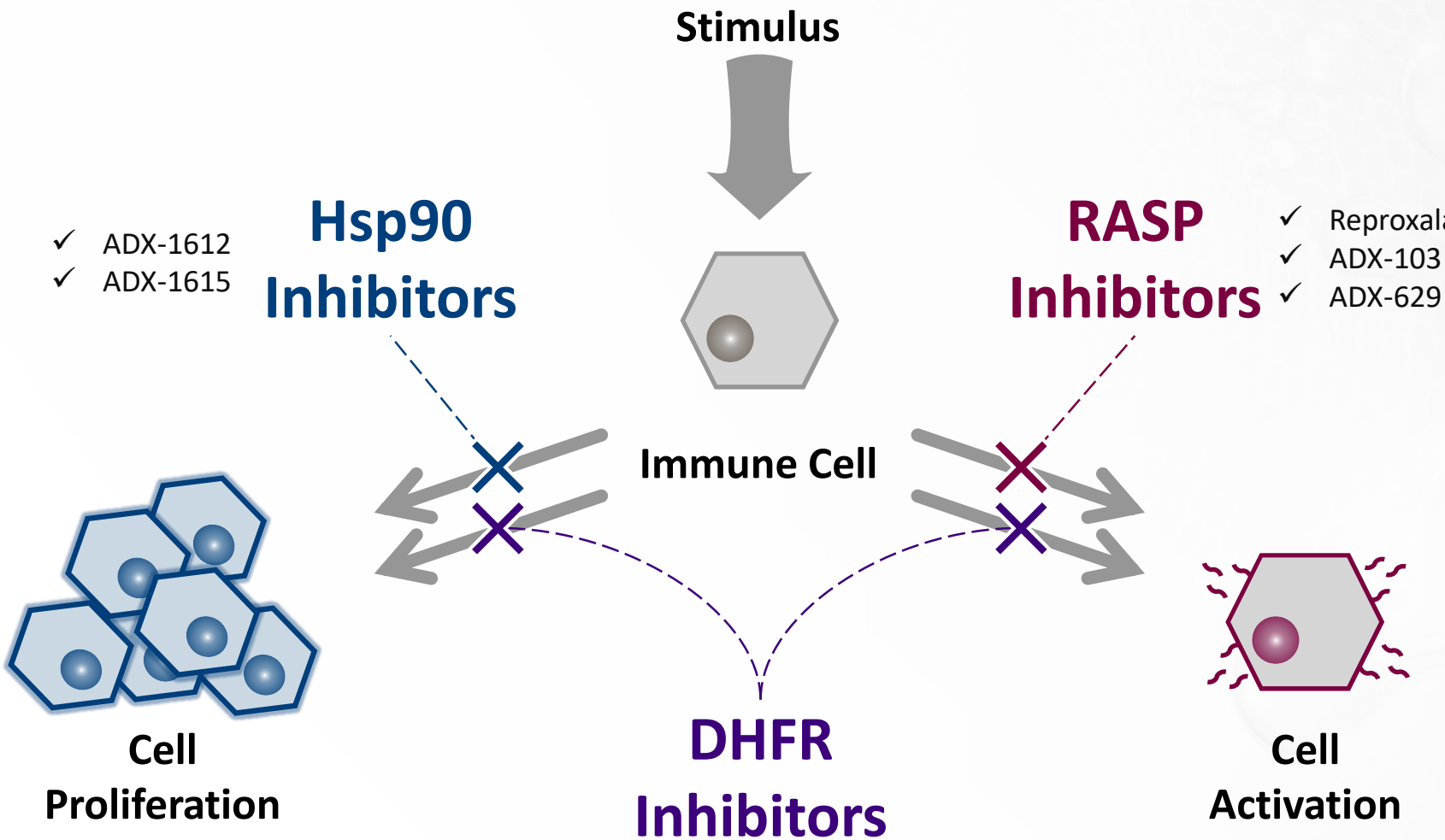
Systemic Diseases

- RASP Sjögren-Larsson Syndrome
- Hsp90 PTLD
- Hsp90 Mesothelioma and other rare cancers**
- RASP Autoimmune

RASP = Reactive Aldehyde Species Inhibitor
DHFR = Dihydrofolate Reductase Inhibitor
Hsp90 = Heat Shock Protein 90 Inhibitor
PTLD = Post-Transplant Lymphoproliferative Disorder
PVR = Proliferative Vitreoretinopathy

*Contingent on funding, regulatory review, and other factors.
**Initially supporting Investigator Sponsored Trials upon Hsp90 licensure.

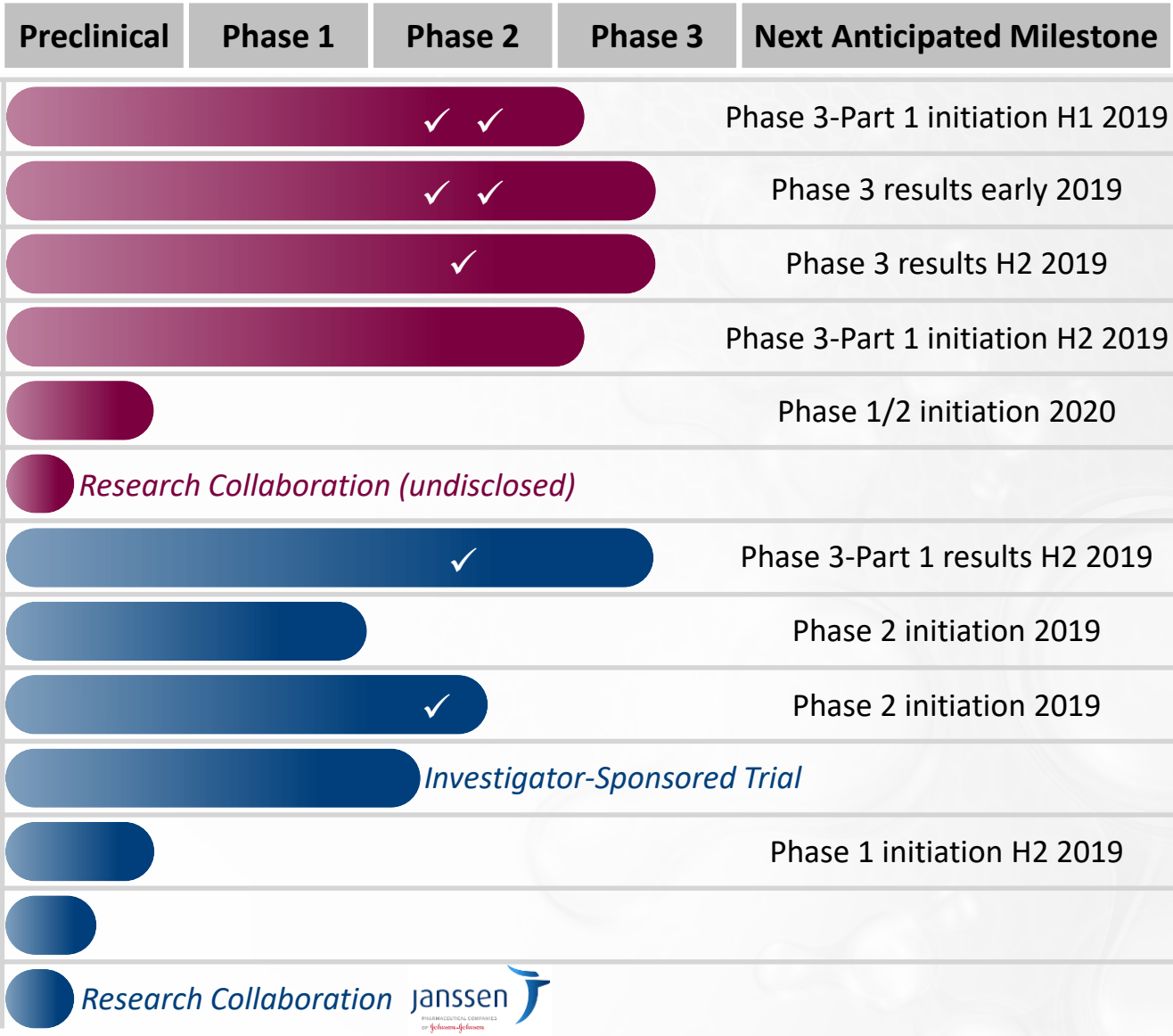
Our Novel Approaches to Address Immune-Mediated Disease



RASP = Reactive Aldehyde Species
DHFR = Dihydrofolate Reductase
Hsp90 = Heat Shock Protein 90

Deep and Innovative Pipeline Focused on Immune-Mediated Diseases

Disease Area	Compound	[Mechanism]	Indication	Next Anticipated Milestone
Ocular Diseases	Reproxalap	[RASP]	Dry Eye Disease	Phase 3-Part 1 initiation H1 2019
			Allergic Conjunctivitis	Phase 3 results early 2019
			Noninfectious Anterior Uveitis	Phase 3 results H2 2019
	ADX-2191	[DHFR]	Proliferative Vitreoretinopathy	Phase 3-Part 1 initiation H2 2019
	ADX-103	[RASP]	Retinal Disease	Phase 1/2 initiation 2020
	Undisclosed		Ocular Inflammation	*Research Collaboration (undisclosed)*
Systemic Diseases	Reproxalap	[RASP]	Sjögren-Larsson Syndrome	Phase 3-Part 1 results H2 2019
	ADX-1612	[Hsp90]	PTLD	Phase 2 initiation 2019
			Mesothelioma	Phase 2 initiation 2019
			Ovarian Cancer	*Investigator-Sponsored Trial*
	ADX-629	[RASP]	Autoimmune Disease	Phase 1 initiation H2 2019
	ADX-1615	[Hsp90]	Autoimmune Disease / Cancer	
	Undisclosed	[RASP]	Systemic Inflammatory Disease	*Research Collaboration* Janssen



RASP = Reactive Aldehyde Species Inhibitor
DHFR = Dihydrofolate Reductase Inhibitor
Hsp90 = Heat Shock Protein 90 Inhibitor
PTLD = Post-Transplant Lymphoproliferative Disorder

✓ = Positive Phase 2 clinical trial data reported in 2016 – 2018
Trial initiations contingent on funding, regulatory review, and other factors

Helio Vision Acquisition Expands Pipeline in Support of Our Strategic Growth Plans

- **Retinal disease a strategic priority** for pipeline growth
- **Novel therapeutic approach** leveraging an immunological mechanism that diminishes inflammation and cell proliferation
- Addition of **Phase 3-ready clinical program**
- **Orphan drug designation** for proliferative vitreoretinopathy, a potentially blinding disease with **no approved treatment**
- Potential **applicability to a variety of other diseases**

Proliferative Vitreoretinopathy – A Rare Retinal Disease

Dean Eliott, M.D.
Professor of Ophthalmology at
Harvard Medical School, and Director of the Retina Service at
Massachusetts Eye and Ear Infirmary

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Multiple Intravitreal Injections of Methotrexate for the Prevention of Proliferative Vitreoretinopathy

Proliferative Vitreoretinopathy (PVR)

A severe scarring condition that develops after retinal detachment surgery

Proliferative Vitreoretinopathy (PVR)

A severe scarring condition that develops after retinal detachment surgery

The leading cause of failure after retinal detachment surgery

Proliferative Vitreoretinopathy (PVR)

A severe scarring condition that develops after retinal detachment surgery

The leading cause of failure after retinal detachment surgery

PVR is an unsolved problem

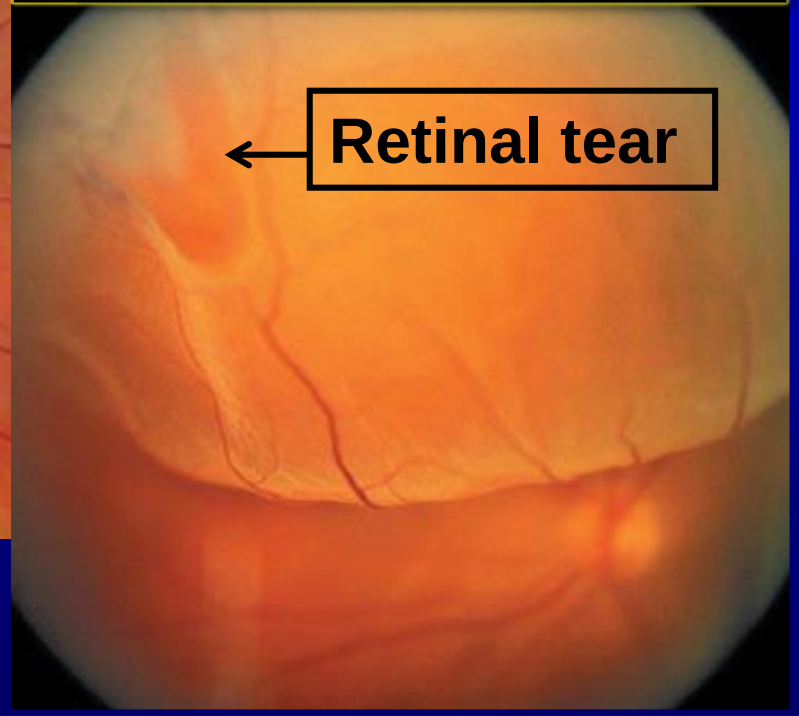
Proliferative Vitreoretinopathy (PVR)

Normal Retina

Proliferative Vitreoretinopathy (PVR)

Normal Retina

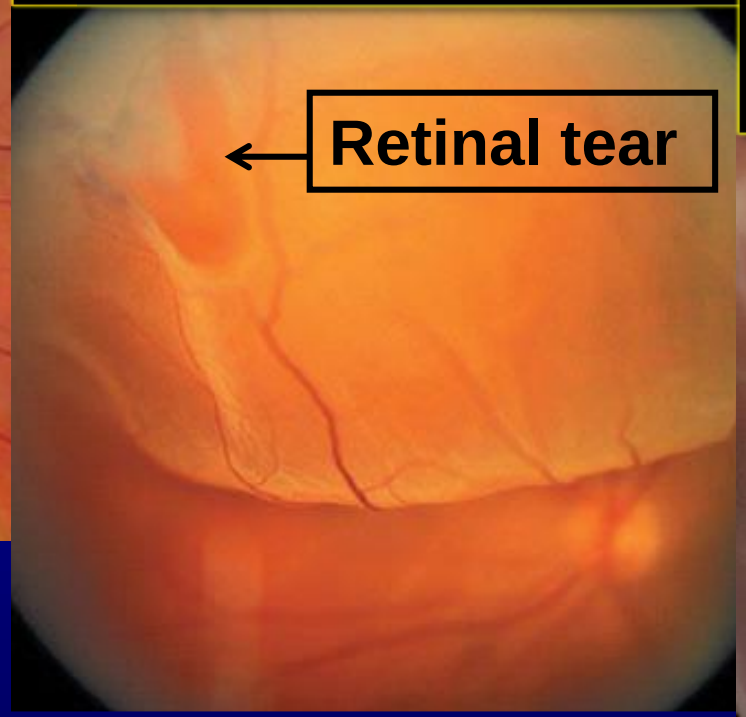
Retinal Detachment



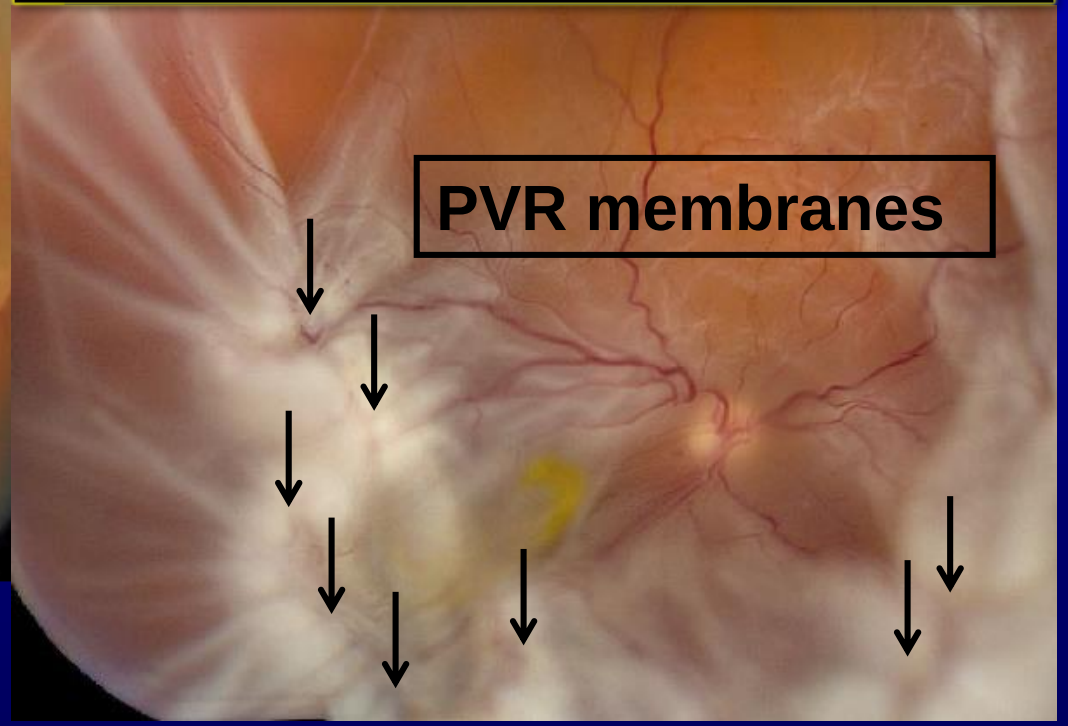
Proliferative Vitreoretinopathy (PVR)

Normal Retina

Retinal Detachment

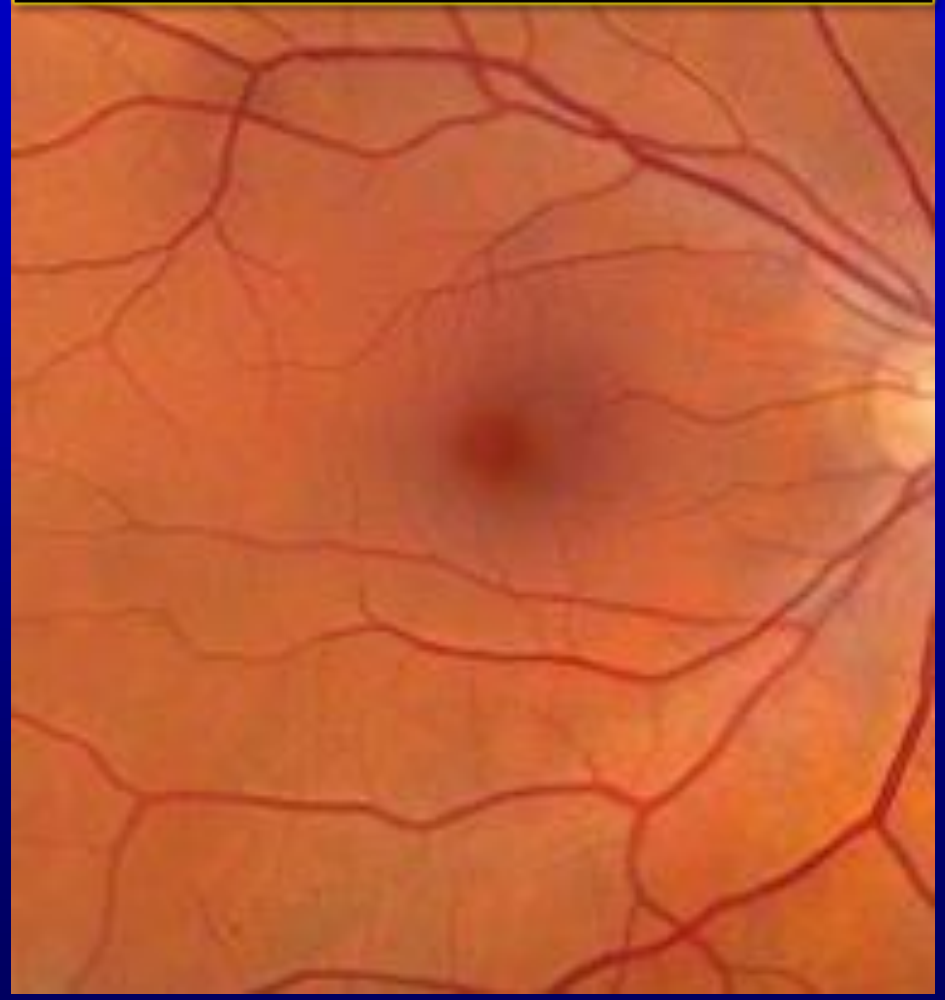


Recurrent Retinal Detachment due to PVR

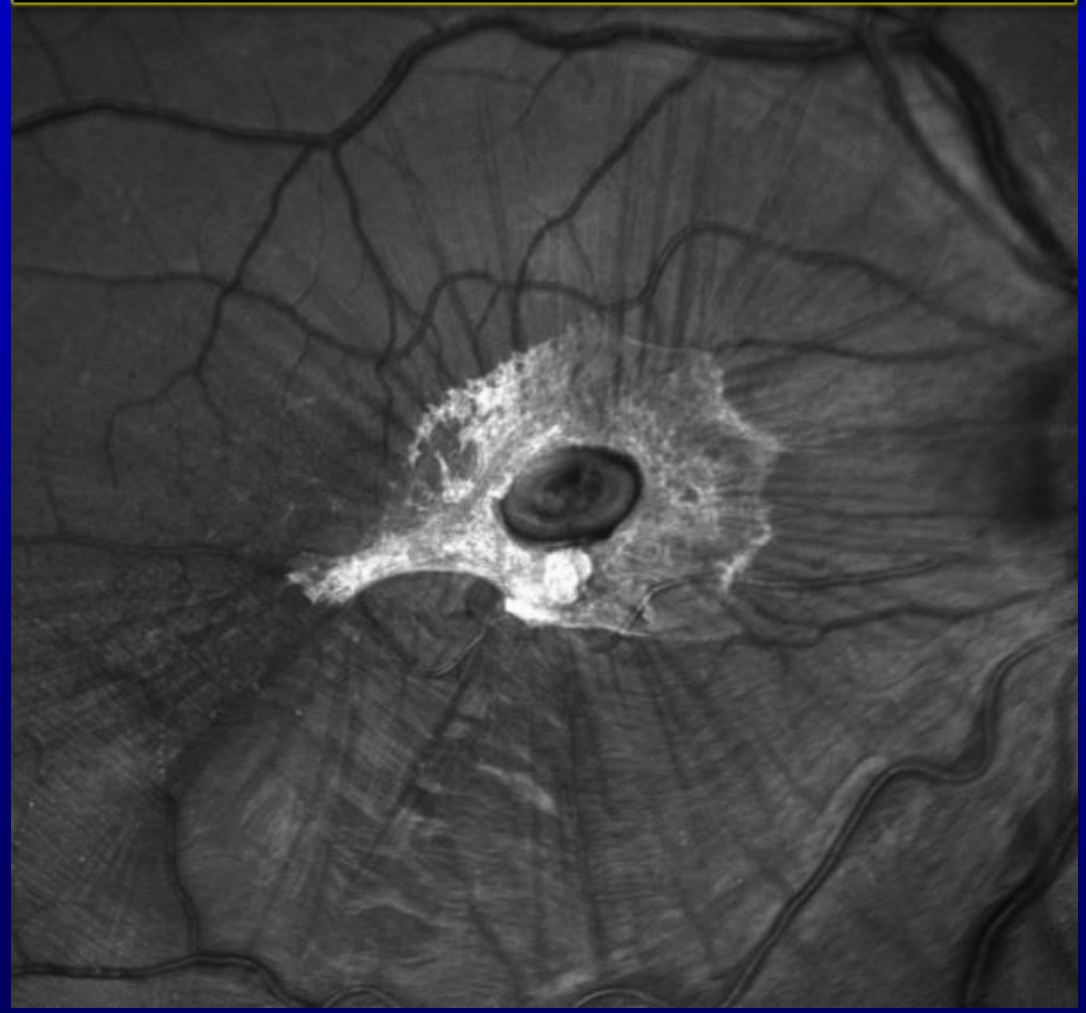


Epiretinal Membrane

Normal Retina



Epiretinal Membrane



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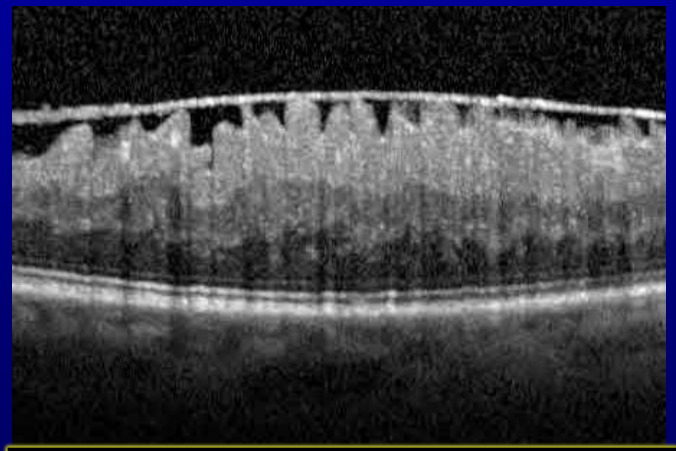
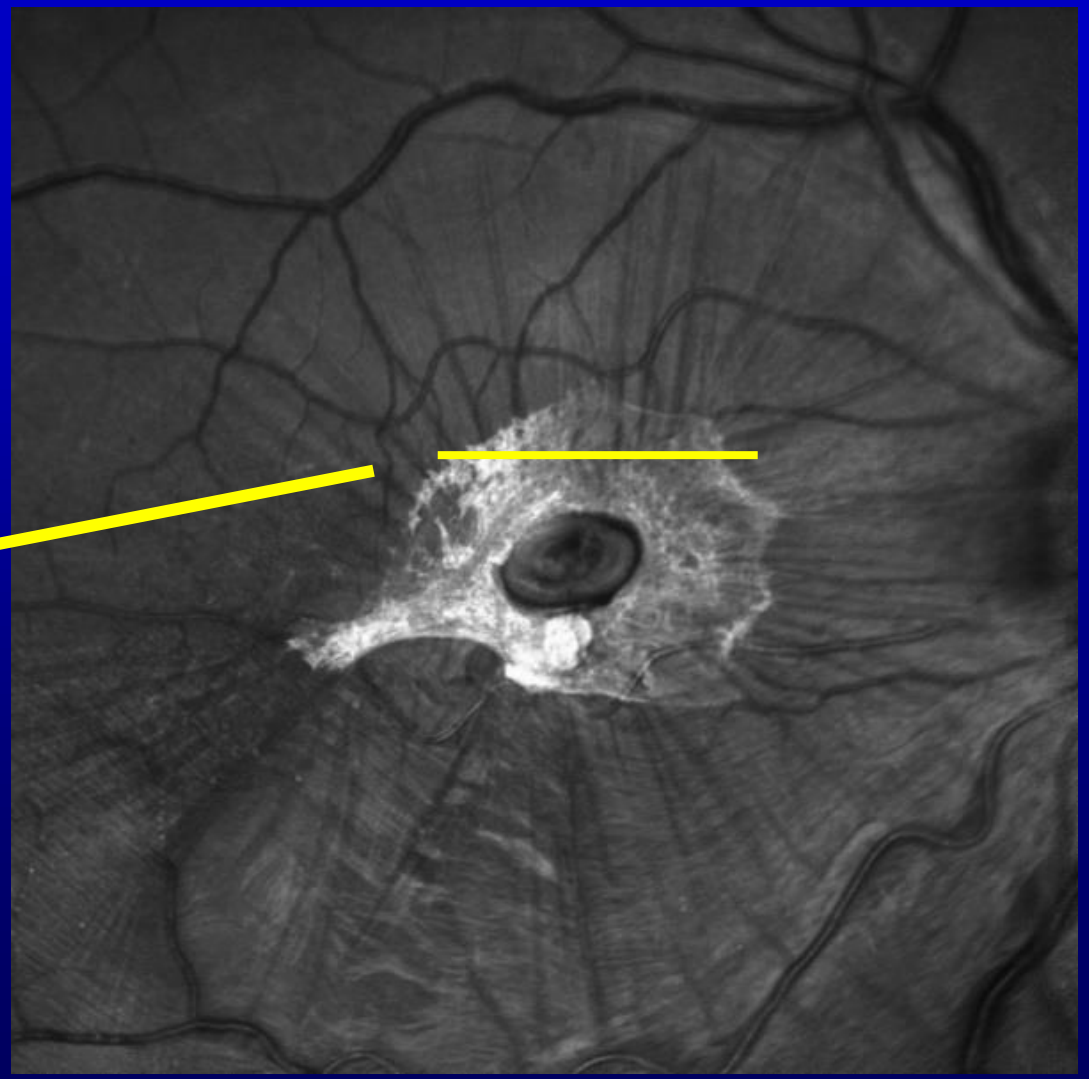


OCT scan (cross section)



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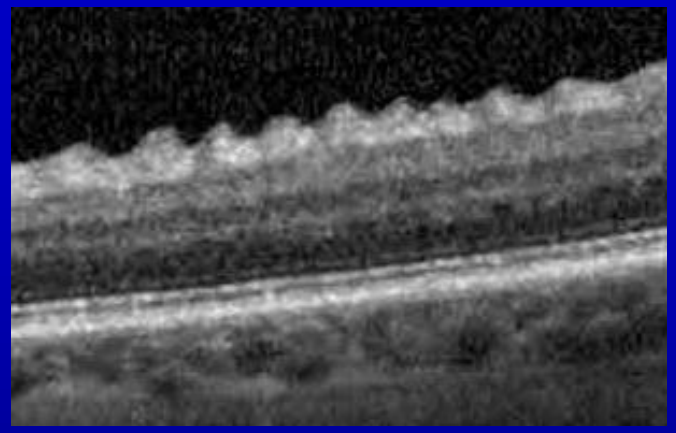

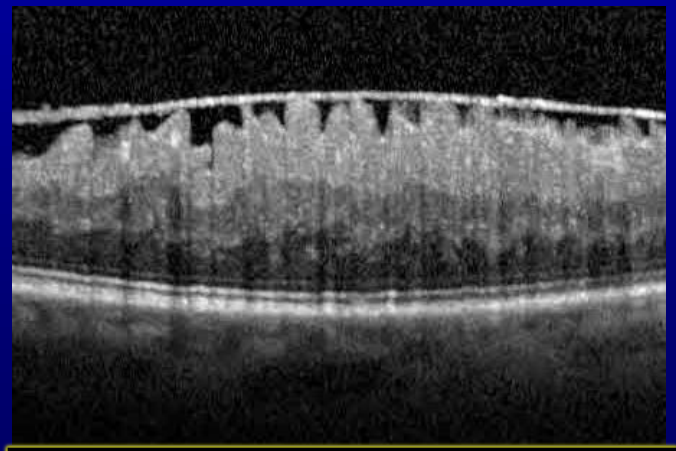

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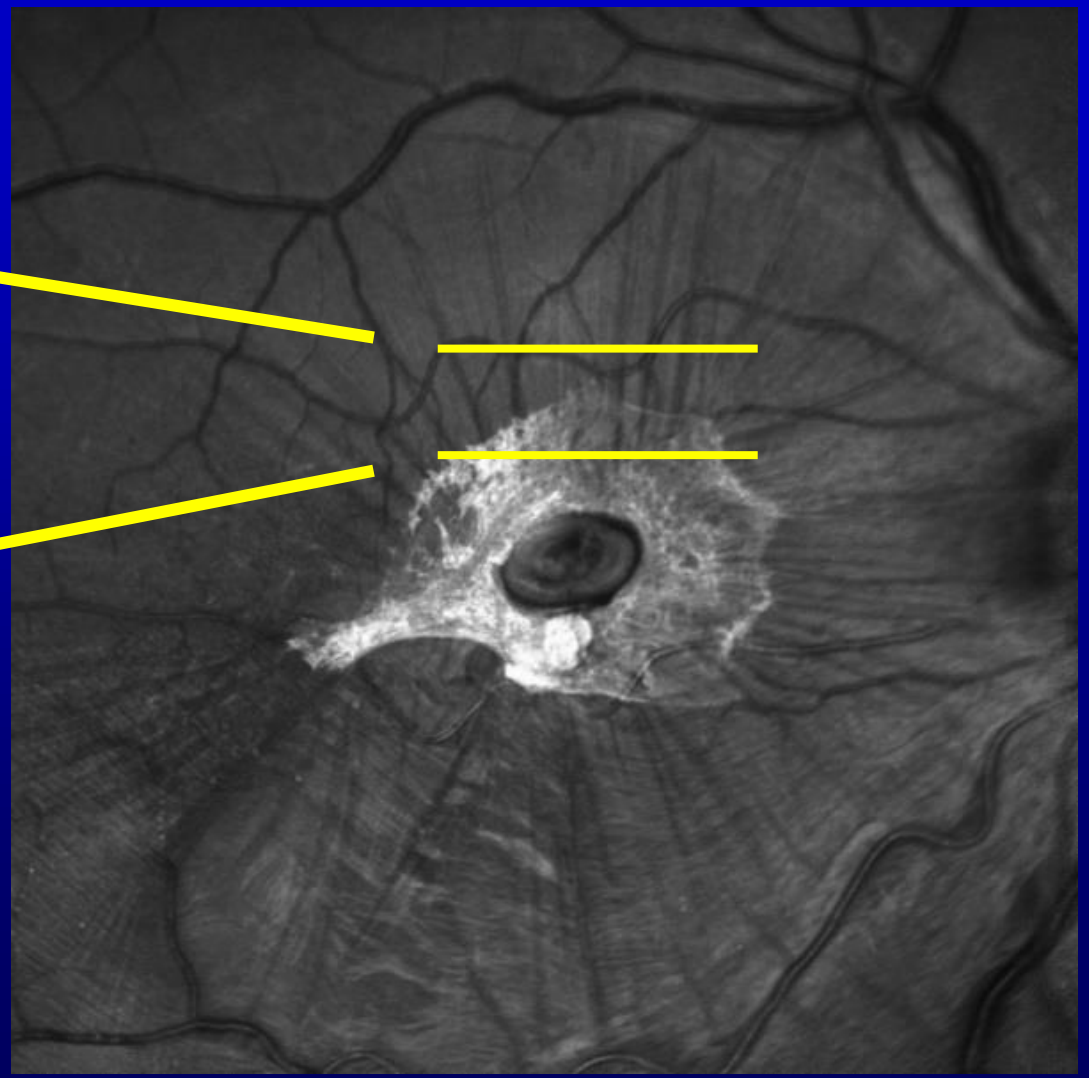
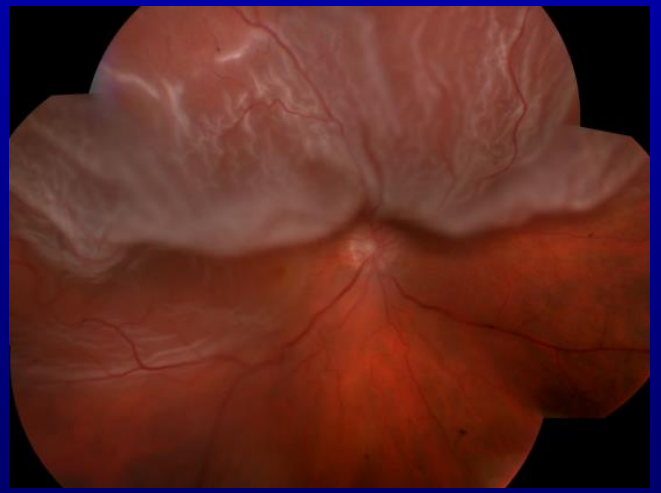


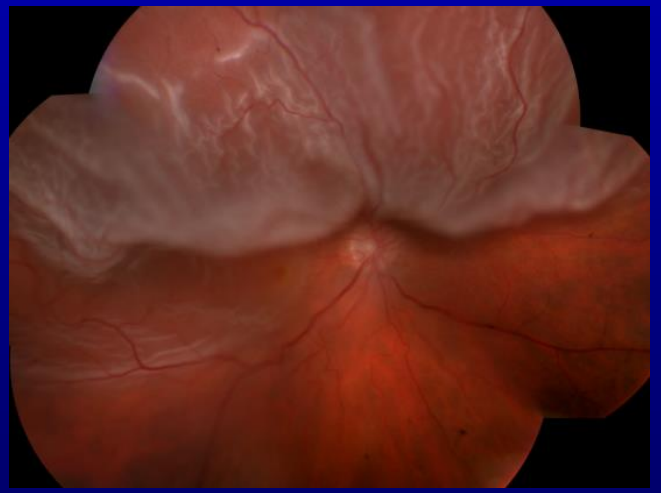
Who gets PVR?

Primary Retinal Detachment



Who gets PVR?

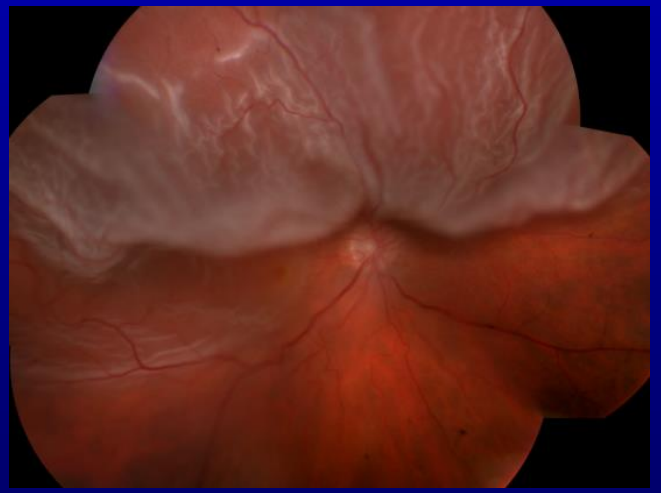
Primary Retinal Detachment



Surgery

Who gets PVR?

Primary Retinal Detachment



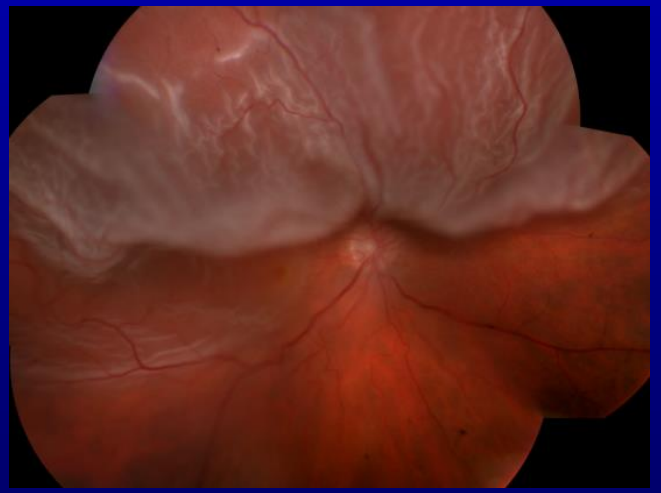
Surgery

Recurrent Retinal Detachment due to PVR

10%

Who gets PVR?

Primary Retinal Detachment



Surgery

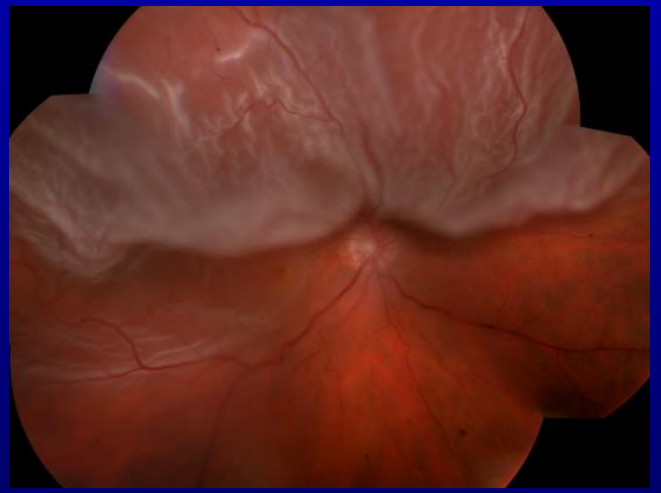
Recurrent Retinal Detachment due to PVR

10%

Up to 50% for high risk cases

Who gets PVR?

Primary Retinal Detachment



Surgery

Recurrent Retinal Detachment due to PVR

10%

Up to 50% for high risk cases

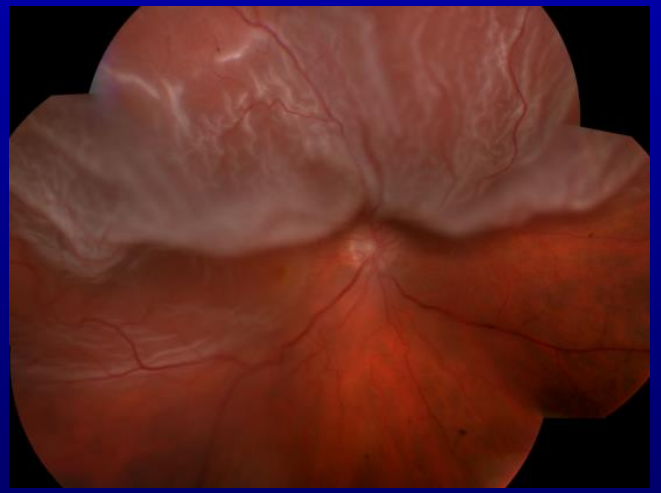
Recurrent Retinal Detachment due to PVR

50%

Who gets PVR?

3.7 surgeries

Primary Retinal Detachment



Surgery

Recurrent Retinal Detachment due to PVR

10%

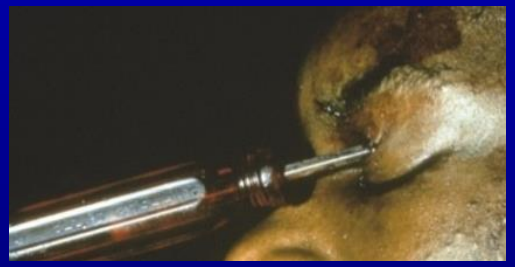
Up to 50% for high risk cases

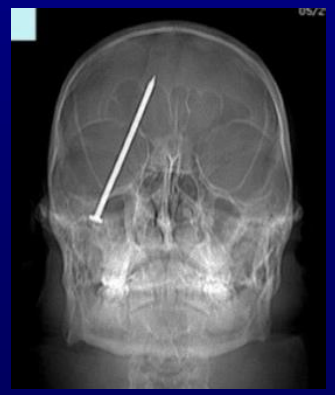
Recurrent Retinal Detachment due to PVR

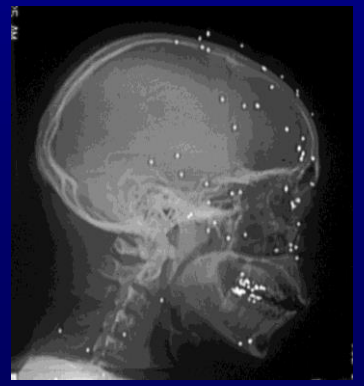
50%

Who gets PVR?

Retinal Detachment Associated with Open Globe Injury

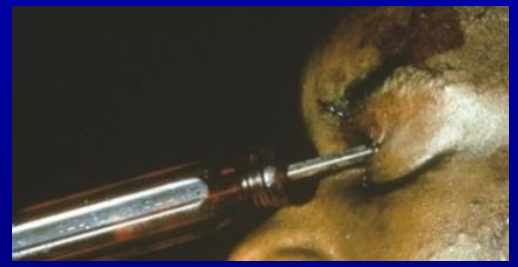


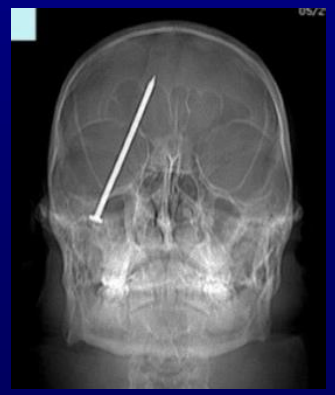



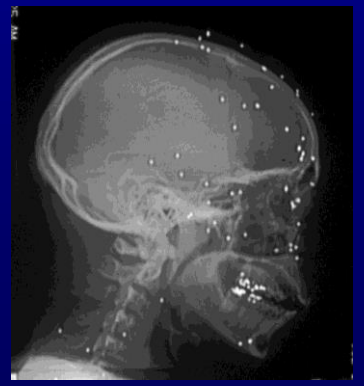
Who gets PVR?

Retinal Detachment Associated with Open Globe Injury



Surgery



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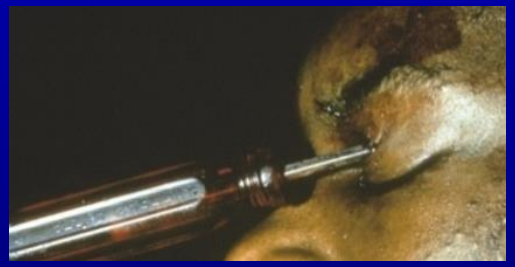


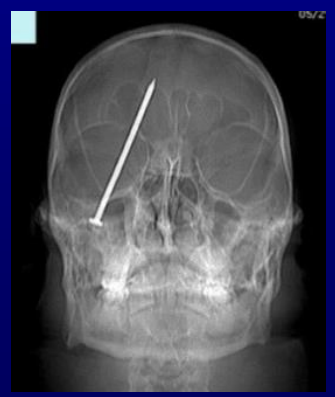


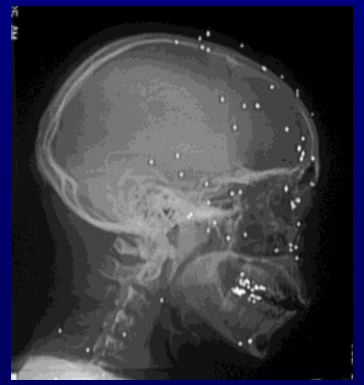

Surgery

Recurrent Retinal Detachment due to PVR

50%

Risk Factors for PVR

Genetics

Ocular Factors

Behavioral Factors

Risk Factors for PVR

Genetics

The *p53* Codon 72 Polymorphism (rs1042522) Is Associated with Proliferative Vitreoretinopathy

The Retina 4 Project

*Salvador Pastor-Idoate, MD,[1,2,3] Irene Rodriguez-Hernández, MSc,[2] Jimena Rojas, MD, PhD,[3] Itziar Fernández, Stc,[3] María Teresa García-Gutierrez, BSc,[3] Jose María Ruiz-Moreno, MD, PhD,[4] Amandio Rocha-Sousa, MD, PhD,[5] Yashin Ramkissoon, PhD, FRCOphth,[6] Steven Harsum, MD, PhD,[6] Robert E. MacLaren, MD, PhD,[6,7] David Charteris, MD, PhD,[6] Jan van Meurs, MD, PhD,[8] Rogelio González-Sarmiento, MD, PhD,[2,9] Jose Carlos Pastor, MD,[1,3] on behalf of the Genetics on PVR Study Group**

A Genetic Case-Control Study Confirms the Implication of *SMAD7* and *TNF Locus* in the Development of Proliferative Vitreoretinopathy

Jimena Rojas,[1] Itziar Fernandez,[2] Jose C. Pastor,[1–3] Robert E. MacLaren,[4] Yashim Ramkissoon,[4] Steven Harsum,[4] David G. Charteris,[4] Jan C. Van Meurs,[5] Sankha Amarakoon,[5] Jose M. Ruiz-Moreno,[6] Amandio Rocha-Sousa,[7] Maria Brion,[8,9] and Angel Carracedo,[8,9] for the Genetics on PVR Study Group[10]

BAX and BCL-2 polymorphisms, as predictors of proliferative vitreoretinopathy development in patients suffering retinal detachment: the Retina 4 project

Salvador Pastor-Idoate,[1,2] Irene Rodríguez-Hernández,[2,3] Jimena Rojas,[1] Itziar Fernández,[1] María-Teresa García-Gutierrez,[1] Jose M. Ruiz-Moreno,[4] Amandio Rocha-Sousa,[5] Yashin D. Ramkissoon,[6,7] Steven Harsum,[6] Robert E. MacLaren,[6,8] David G. Charteris,[6] Jan C. Van Meurs,[9] Rogelio González-Sarmiento,[2,3] and Jose C. Pastor[1] on behalf of the Genetics on PVR Study Group

The T309G MDM2 Gene Polymorphism Is a Novel Risk Factor for Proliferative Vitreoretinopathy

Salvador Pastor-Idoate[1,2], Irene Rodríguez-Hernández[2,3], Jimena Rojas[1], Itziar Fernández[1], María T. García-Gutiérrez[1], José M. Ruiz-Moreno[4], Amandio Rocha-Sousa[5], Yashin Ramkissoon[6], Steven Harsum[6], Robert E. MacLaren[6,7], David Charteris[6], Jan C. VanMeurs[8], Rogelio González-Sarmiento[2,3]*, José C. Pastor[1]*, on behalf of the Genetics on PVR Study Group[1]

Ocular Factors

Behavioral Factors

Risk Factors for PVR

Genetics

The *p53* Codon 72 Polymorphism (rs1042522) Is Associated with Proliferative Vitreoretinopathy

The Retina 4 Project

*Salvador Pastor-Idoate, MD,[1,2,3] Irene Rodriguez-Hernández, MSc,[2] Jimena Rojas, MD, PhD,[3] Itziar Fernández, Stc,[3] María Teresa García-Gutierrez, BSc,[3] Jose María Ruiz-Moreno, MD, PhD,[4] Amandio Rocha-Sousa, MD, PhD,[5] Yashin Ramkissoon, PhD, FRCOphth,[6] Steven Harsum, MD, PhD,[6] Robert E. MacLaren, MD, PhD,[6,7] David Charteris, MD, PhD,[6] Jan van Meurs, MD, PhD,[8] Rogelio González-Sarmiento, MD, PhD,[2,9] Jose Carlos Pastor, MD,[1,3] on behalf of the Genetics on PVR Study Group**

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Ocular Factors

- post-trauma
- uveitis
- high myopia
- large/giant breaks
- multiple breaks
- vitreous hemorrhage
- choroidal detachment
- early PVR

Behavioral Factors

Risk Factors for PVR

Genetics

The *p53* Codon 72 Polymorphism (rs1042522) Is Associated with Proliferative Vitreoretinopathy

The Retina 4 Project

*Salvador Pastor-Idoate, MD,[1,2,3] Irene Rodriguez-Hernández, MSc,[2] Jimena Rojas, MD, PhD,[3] Itziar Fernández, Stc,[3] María Teresa García-Gutierrez, BSc,[3] Jose María Ruiz-Moreno, MD, PhD,[4] Amandio Rocha-Sousa, MD, PhD,[5] Yashin Ramkissoon, PhD, FRCOphth,[6] Steven Harsum, MD, PhD,[6] Robert E. MacLaren, MD, PhD,[6,7] David Charteris, MD, PhD,[6] Jan van Meurs, MD, PhD,[8] Rogelio González-Sarmiento, MD, PhD,[2,9] Jose Carlos Pastor, MD,[1,3] on behalf of the Genetics on PVR Study Group**

A Genetic Case-Control Study Confirms the Implication of *SMAD7* and *TNF Locus* in the Development of Proliferative Vitreoretinopathy

Jimena Rojas,[1] Itziar Fernandez,[2] Jose C. Pastor,[1–3] Robert E. MacLaren,[4] Yashim Ramkissoon,[4] Steven Harsum,[4] David G. Charteris,[4] Jan C. Van Meurs,[5] Sankha Amarakoon,[5] Jose M. Ruiz-Moreno,[6] Amandio Rocha-Sousa,[7] Maria Brion,[8,9] and Angel Carracedo,[8,9] for the Genetics on PVR Study Group[10]

BAX and BCL-2 polymorphisms, as predictors of proliferative vitreoretinopathy development in patients suffering retinal detachment: the Retina 4 project

Salvador Pastor-Idoate,[1,2] Irene Rodríguez-Hernández,[2,3] Jimena Rojas,[1] Itziar Fernández,[1] María-Teresa García-Gutierrez,[1] Jose M. Ruiz-Moreno,[4] Amandio Rocha-Sousa,[5] Yashin D. Ramkissoon,[6,7] Steven Harsum,[6] Robert E. MacLaren,[6,8] David G. Charteris,[6] Jan C. Van Meurs,[9] Rogelio González-Sarmiento,[2,3] and Jose C. Pastor[1] on behalf of the Genetics on PVR Study Group

The T309G MDM2 Gene Polymorphism Is a Novel Risk Factor for Proliferative Vitreoretinopathy

Salvador Pastor-Idoate[1,2], Irene Rodríguez-Hernández[2,3], Jimena Rojas[1], Itziar Fernández[1], María T. García-Gutiérrez[1], José M. Ruiz-Moreno[4], Amandio Rocha-Sousa[5], Yashin Ramkissoon[6], Steven Harsum[6], Robert E. MacLaren[6,7], David Charteris[6], Jan C. VanMeurs[8], Rogelio González-Sarmiento[2,3]*, José C. Pastor[1]*, on behalf of the Genetics on PVR Study Group[1]

Ocular Factors

- post-trauma
- uveitis
- high myopia
- large/giant breaks
- multiple breaks
- vitreous hemorrhage
- choroidal detachment
- early PVR

Behavioral Factors

SMOKING IS A RISK FACTOR FOR PROLIFERATIVE VITREORETINOPATHY AFTER TRAUMATIC RETINAL DETACHMENT

DEAN ELIOTT, MD,*† TOMASZ P. STRYJEWSKI, MD, MPP,*† MICHAEL T. ANDREOLI, MD,‡ CHRISTOPHER M. ANDREOLI, MD*‡§

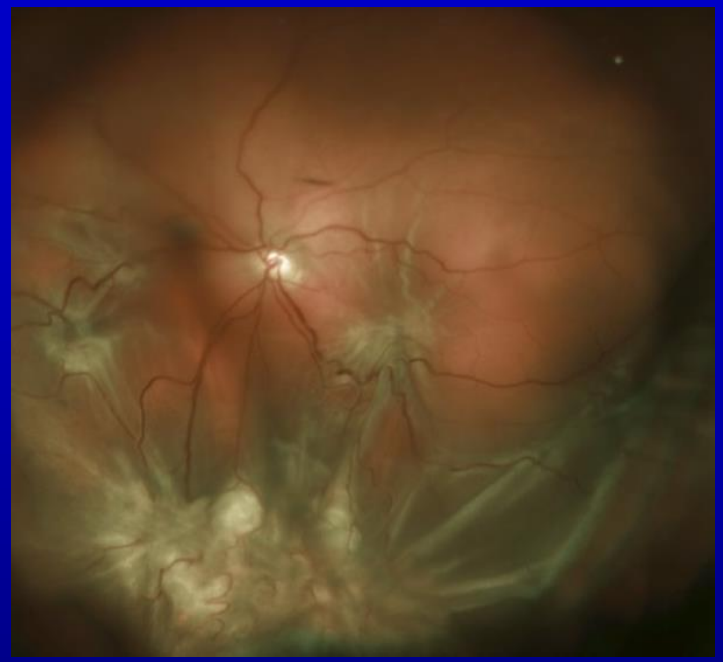
PREDICTIVE FACTORS FOR PROLIFERATIVE VITREORETINOPATHY FORMATION AFTER UNCOMPLICATED PRIMARY RETINAL DETACHMENT REPAIR

KUNYONG XU, MD, MHSc,* ERIC K. CHIN, MD,† STEVEN R. BENNETT, MD,‡ DAVID F. WILLIAMS, MD, MBA,‡ EDWIN H. RYAN, MD,‡ SUNDEEP DEV, MD,‡ ROBERT A. MITTRA, MD,‡ POLLY A. QUIRAM, MD, PhD,‡ JOHN B. DAVIES, MD,‡ DAVID WILKIN PARKE III, MD,‡ HERBERT CULVER BOLDT, MD,§ DAVID R. P. ALMEIDA, MD, MBA, PhD‡

Burden of PVR

- Multiple surgeries (average = 3.7)
- Cost (~$8,000/surgery)
- Each retinal detachment results in further permanent visual loss
- Each surgery requires a period of face down positioning

Pharmacologic Trials to Prevent PVR



- Heparin and dexamethasone
- Daunorubicin
- Triamcinolone acetonide
- Prednisone
- 5-Fluorouracil and low-molecular-weight heparin
- Ribozyme to proliferating cell nuclear antigen

Pharmacologic Trials to Prevent PVR

- One-time **injection** at conclusion of surgery

Pharmacologic Trials to Prevent PVR

- One-time **injection** at conclusion of surgery

Triamcinolone Acetonide in Silicone-Filled Eyes as Adjunctive Treatment for Proliferative Vitreoretinopathy

A Randomized Clinical Trial

Hamid Ahmadieh, MD,[1] Mostafa Feghhi, MD,[1] Homa Tabatabaei, MD,[1] Nasser Shoeibi, MD,[1] Alireza Ramezani, MD,[1] Mohammad Reza Mohebbi, MS[1]

Ophthalmology 115:1938-1943,2008

Safety and Efficacy Assessment of Chimeric Ribozyme to Proliferating Cell Nuclear Antigen to Prevent Recurrence of Proliferative Vitreoretinopathy

William M. Schiff, MD; John C. Hwang, MD; Michael D. Ober, MD; Jeffrey L. Olson, MD; Elona Dhrami-Gavazi, MD; Gaetano R. Barile, MD; Stanley Chang, MD; Naresh Mandava, MD; for the IM-VIT100 Study Group

Arch Ophthalmol 125:1161-1167;2007

Pharmacologic Trials to Prevent PVR

- One-time **infusion** during or at conclusion of surgery

Pharmacologic Trials to Prevent PVR

- One-time **infusion** during or at conclusion of surgery

R. Geoff Williams
Stanley Chang
Mark R. Comaratta
George Simoni

Does the presence of heparin and dexamethasone in the vitrectomy infusate reduce reproliferation in proliferative vitreoretinopathy?

Graefe's Arch Clin Exp Oph 234,1996

Adjunctive Daunorubicin in the Treatment of Proliferative Vitreoretinopathy: Results of a Multicenter Clinical Trial

P. WIEDEMANN, MD, R. D. HILGERS, PHD, P. BAUER, PHD, AND K. HEIMANN, MD, FOR THE DAUNOMYCIN STUDY GROUP

Am J Ophthalmol 126:550-559,1998

Pharmacologic Trials to Prevent PVR

- One-time **infusion** during or at conclusion of surgery

Adjuvant 5-fluorouracil and Heparin Prevents Proliferative Vitreoretinopathy

Results from a Randomized, Double-blind, Controlled Clinical Trial

Riaz Hassan Yusuf Asaria, FRCOphth,[1,2] Chee Hing Kon, MD, FRCOphth,[1,2] Catey Bunce, MSc,[3] David G. Charteris, MD, FRCOphth[1,2], David Wong, MD, FRCOphth,[4] Peng Tee Khaw, PhD, FRCOphth,[1,2] George William Aylward, MD, FRCOphth[1,2]

Ophthalmology 108:1179-1183,2001

A Randomized Controlled Trial of Combined 5-Fluorouracil and Low-Molecular-Weight Heparin in Management of Established Proliferative Vitreoretinopathy

*David G. Charteris, MD, FRCS (Ed),[1] G. William Aylward, MD, FRCS,[1] David Wong, FRCS, FRCOphth,[2] Carl Groenewald, FRCS, FRCOphth,[2] Riaz H. Y. Asaria, MD, FRCS,[1] Catey Bunce, DSc,[3] for the PVR Study Group**

Ophthalmology 111:2240-2245,2004

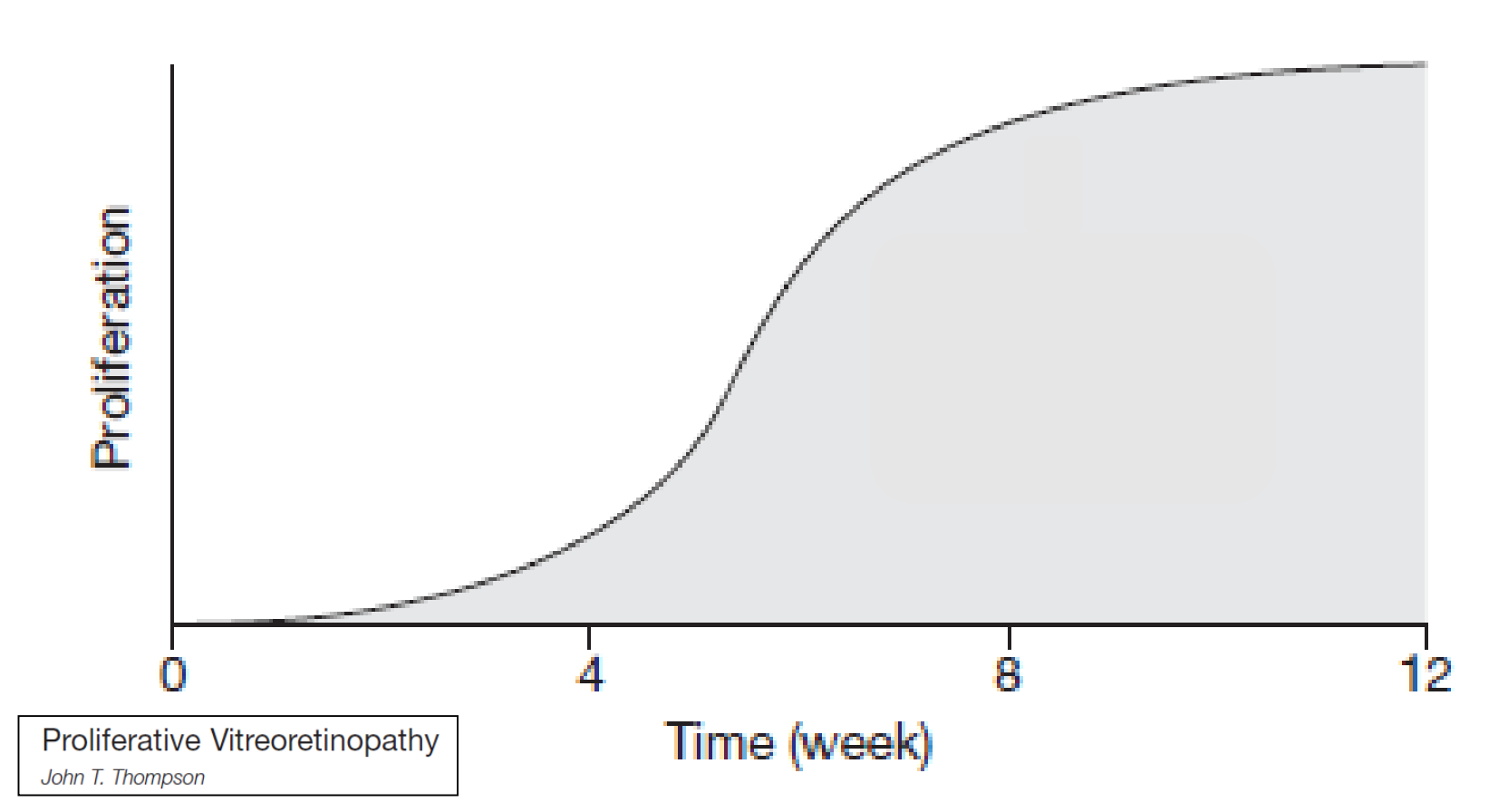
Randomized Controlled Trial of Combined 5-Fluorouracil and Low-Molecular-Weight Heparin in the Management of Unselected Rhegmatogenous Retinal Detachments Undergoing Primary Vitrectomy

L. Wickham, MBBS, MRCOphth,[1] C. Bunce, MSc, DSc,[1] D. Wong, FRCS, FRCOphth,[2] D. McGurn, RGN,[1] D. G. Charteris, FRCS(Ed), FRCOphth[1]

Ophthalmology 114:698-704,2007

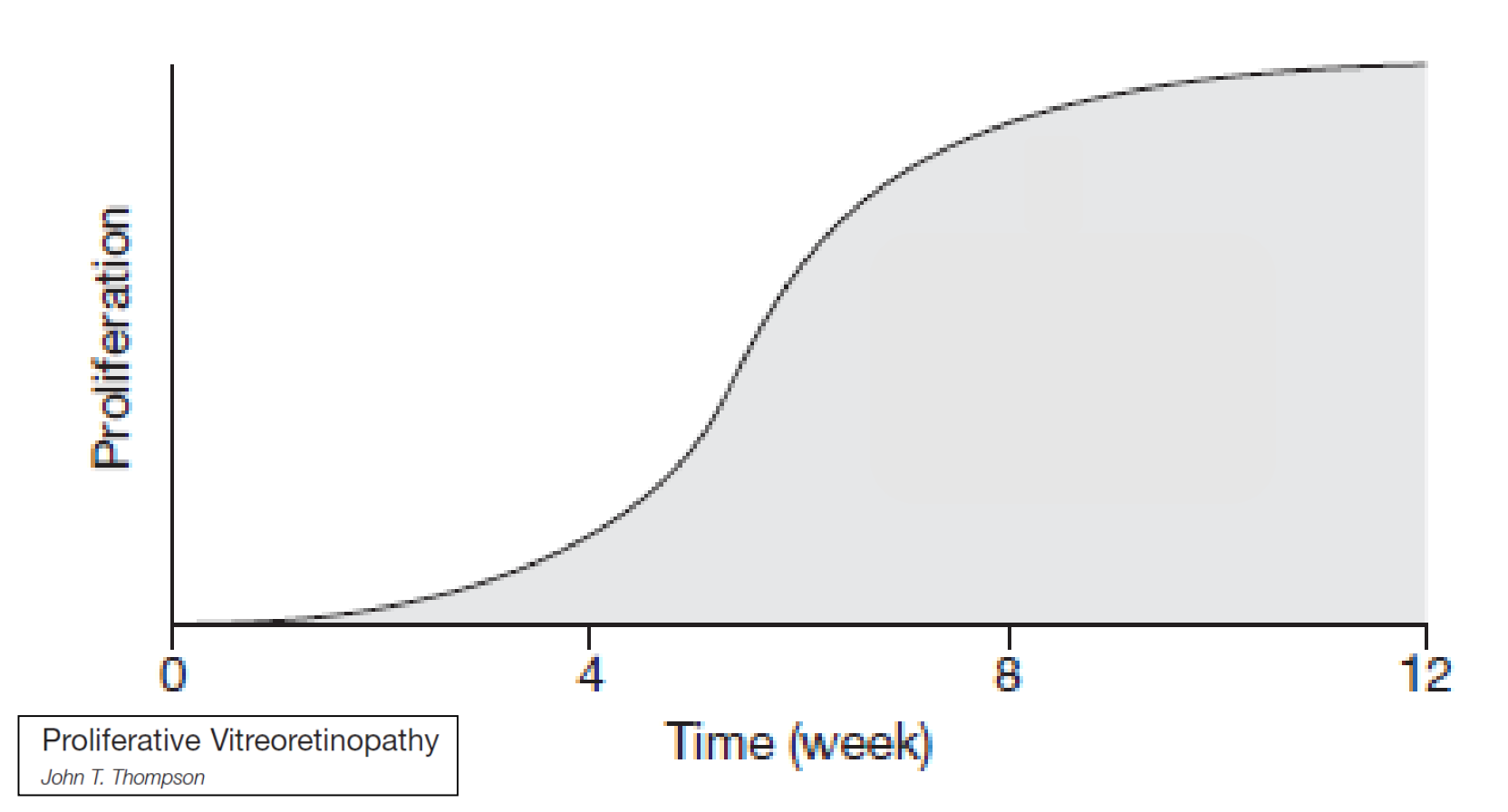
Clinical Development of PVR

PVR peaks 2-3 months

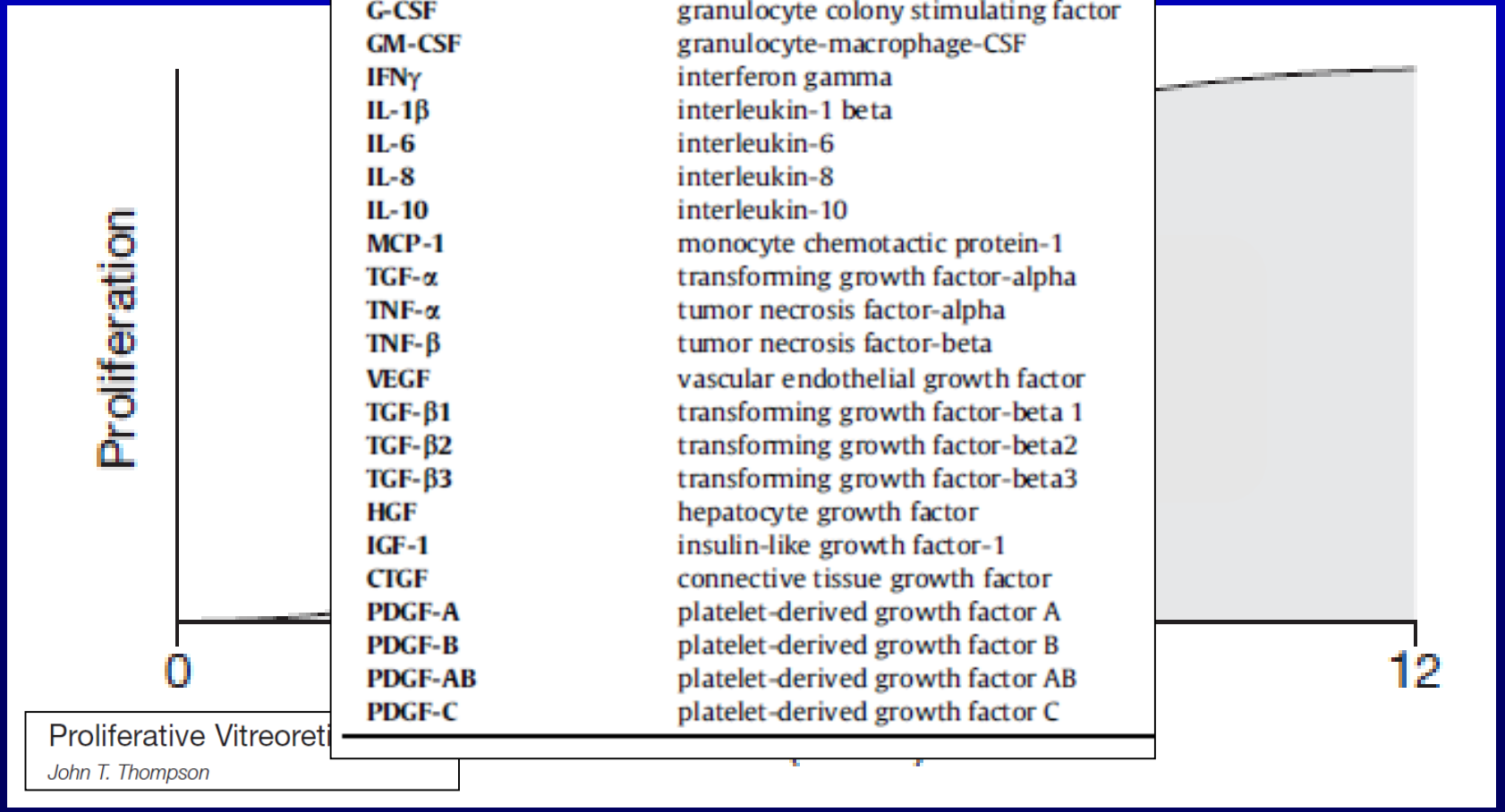


Clinical Development of PVR

PVR peaks earlier in open globe injury cases



Clinical Development of PVR

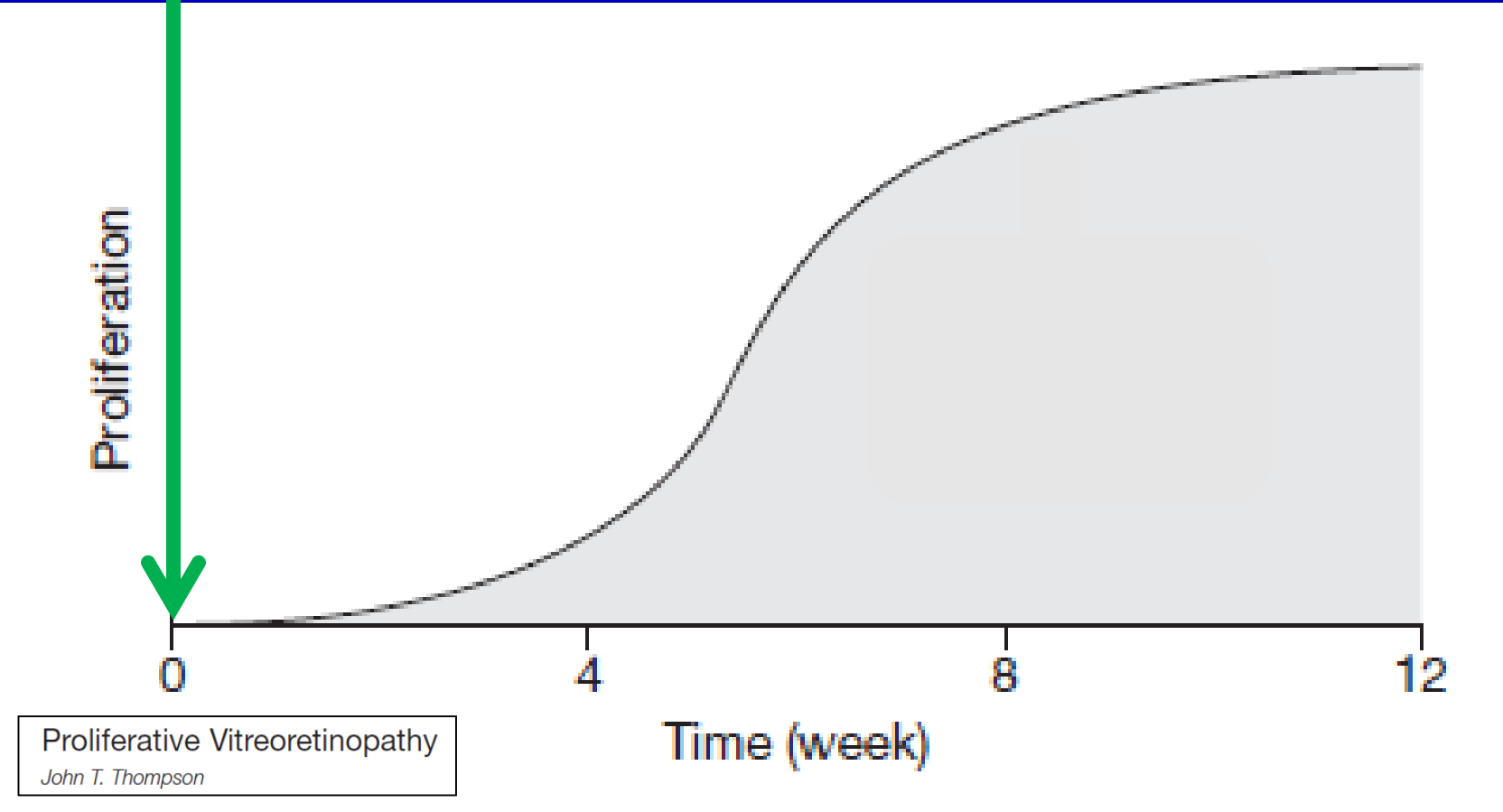


Growth factors and cytokines that are implicated in PVR.

Growth factor/cytokine	
EGF	epidermal growth factor
FGF-2	fibroblast growth factor-2
G-CSF	granulocyte colony stimulating factor
GM-CSF	granulocyte-macrophage-CSF
IFNγ	interferon gamma
IL-1β	interleukin-1 beta
IL-6	interleukin-6
IL-8	interleukin-8
IL-10	interleukin-10
MCP-1	monocyte chemotactic protein-1
TGF-α	transforming growth factor-alpha
TNF-α	tumor necrosis factor-alpha
TNF-β	tumor necrosis factor-beta
VEGF	vascular endothelial growth factor
TGF-β1	transforming growth factor-beta 1
TGF-β2	transforming growth factor-beta2
TGF-β3	transforming growth factor-beta3
HGF	hepatocyte growth factor
IGF-1	insulin-like growth factor-1
CTGF	connective tissue growth factor
PDGF-A	platelet-derived growth factor A
PDGF-B	platelet-derived growth factor B
PDGF-AB	platelet-derived growth factor AB
PDGF-C	platelet-derived growth factor C

Clinical Development of PVR

one-time exposure



Clinical Development of PVR

one-time exposure

inhibit all of these factors

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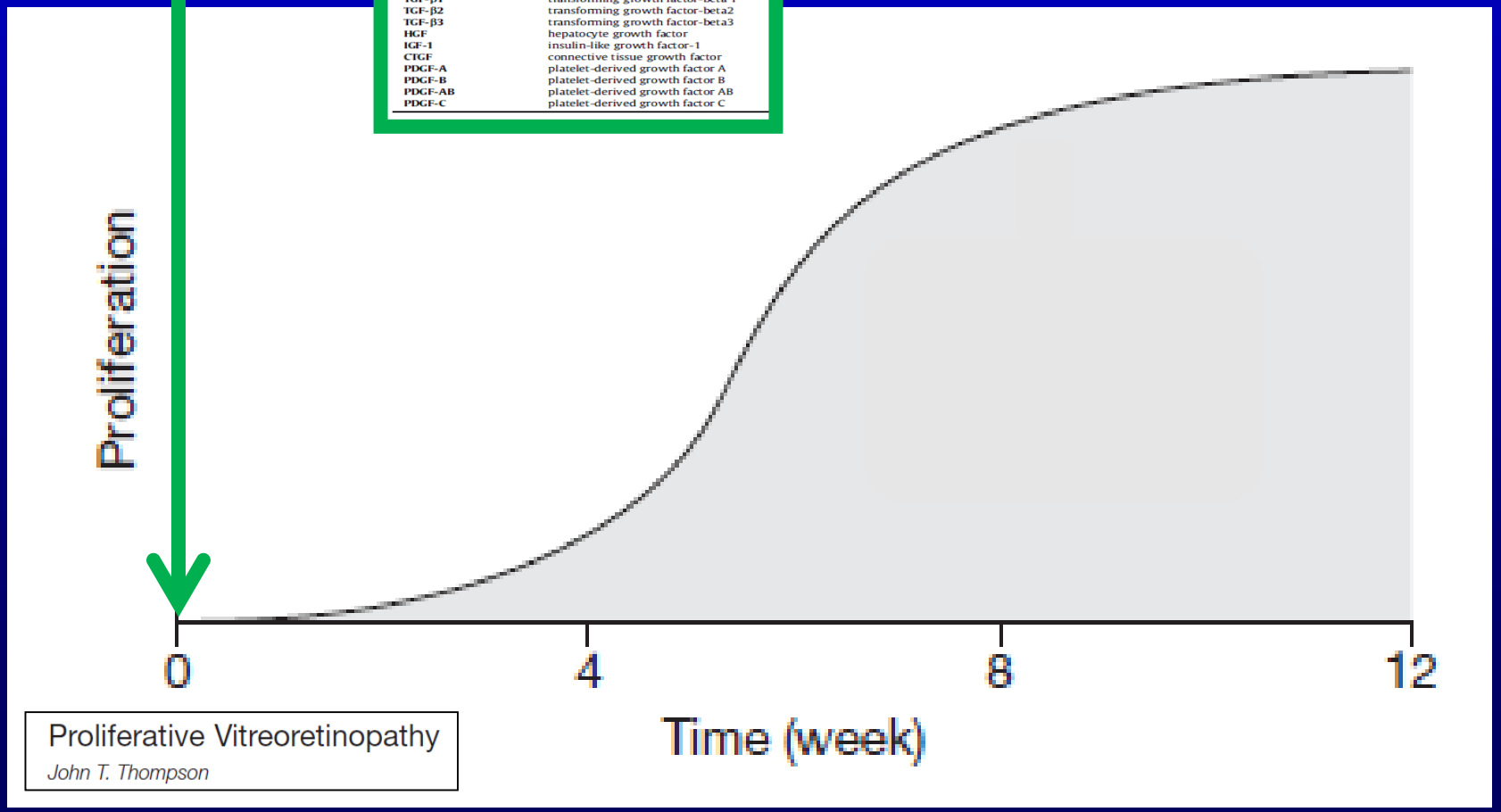

Clinical Development of PVR

one-time exposure

inhibit all of these factors

sustained over this entire time

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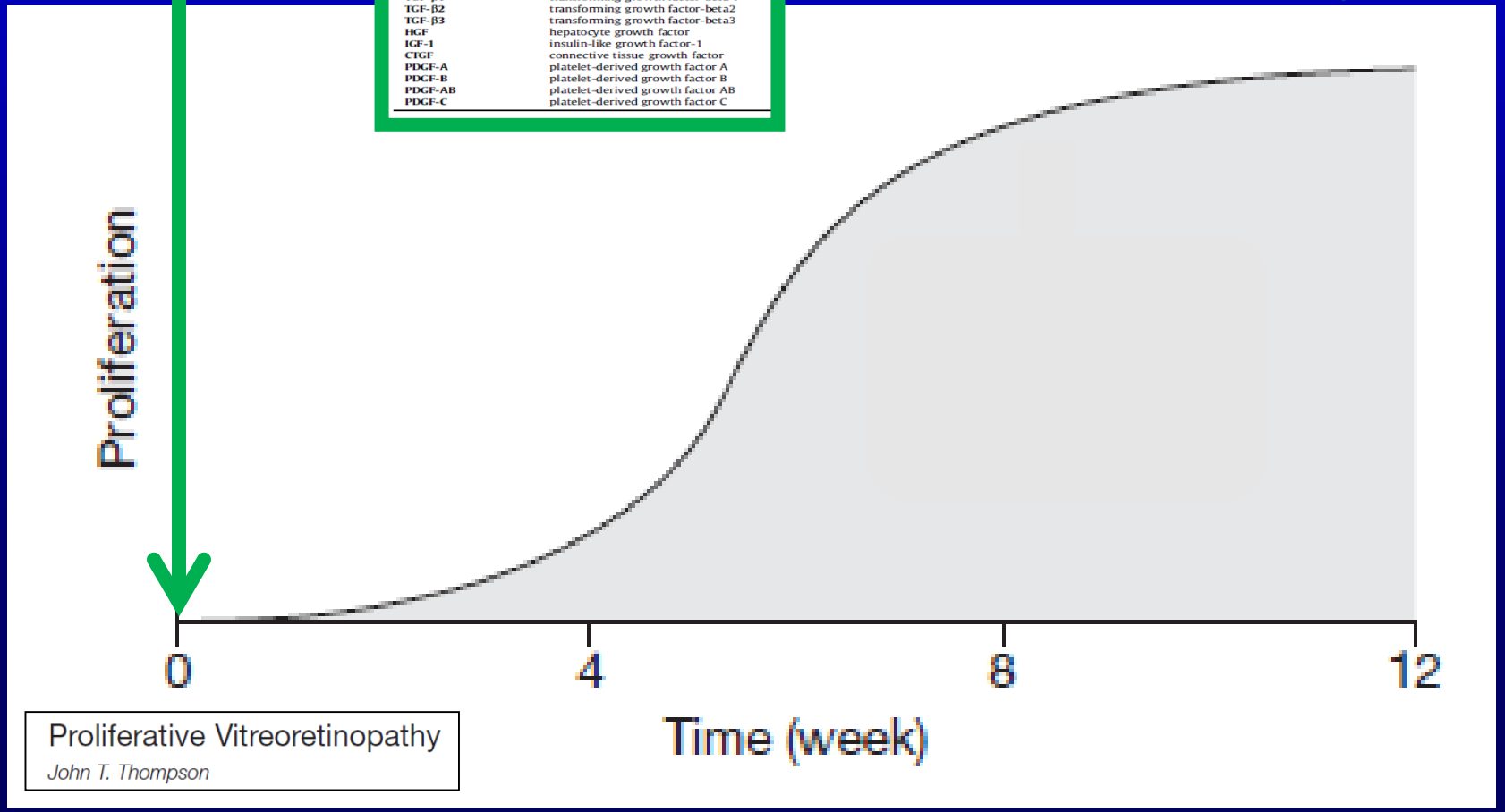

Clinical Development of PVR

one-time exposure

inhibit all of these factors

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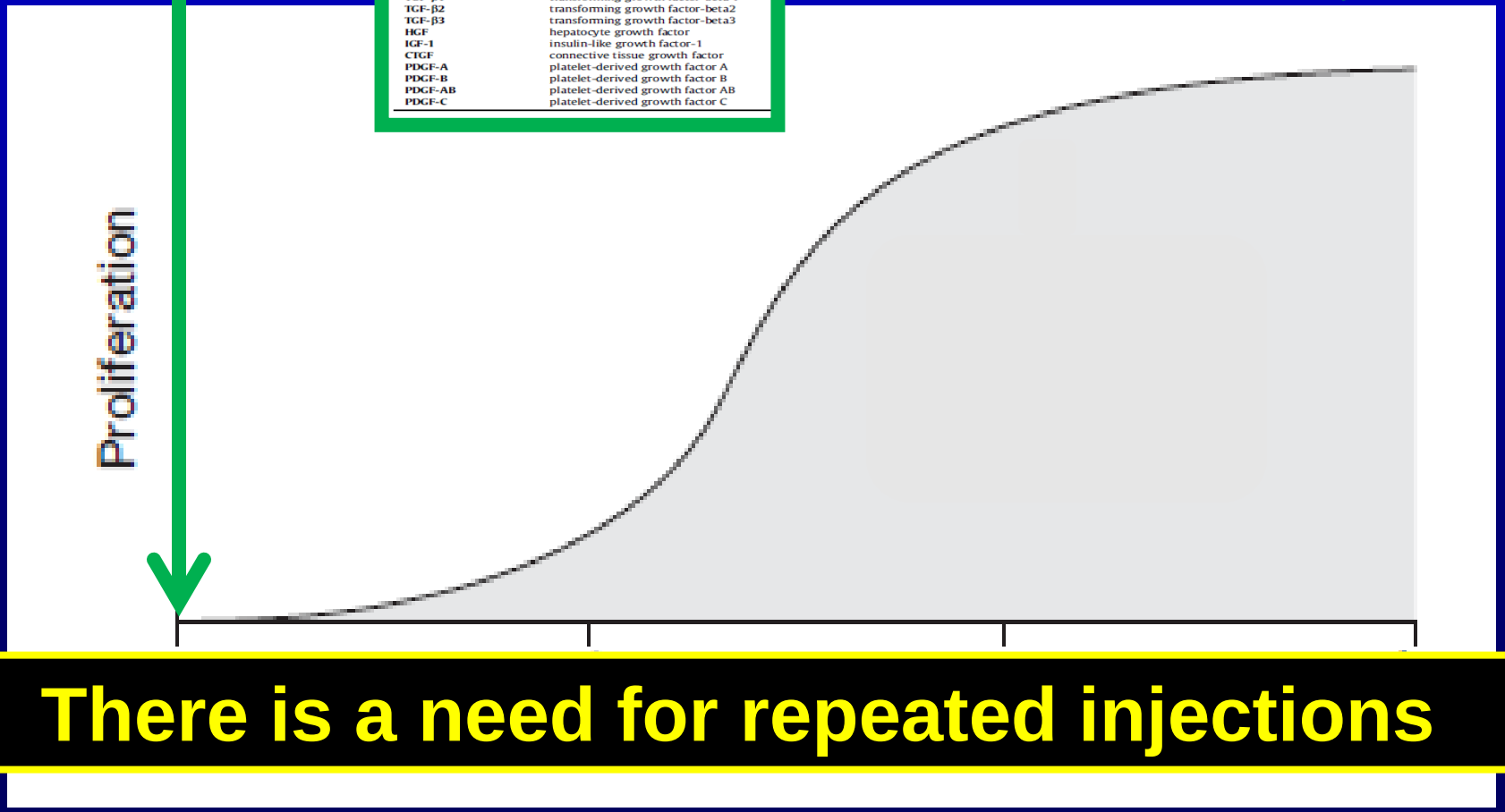
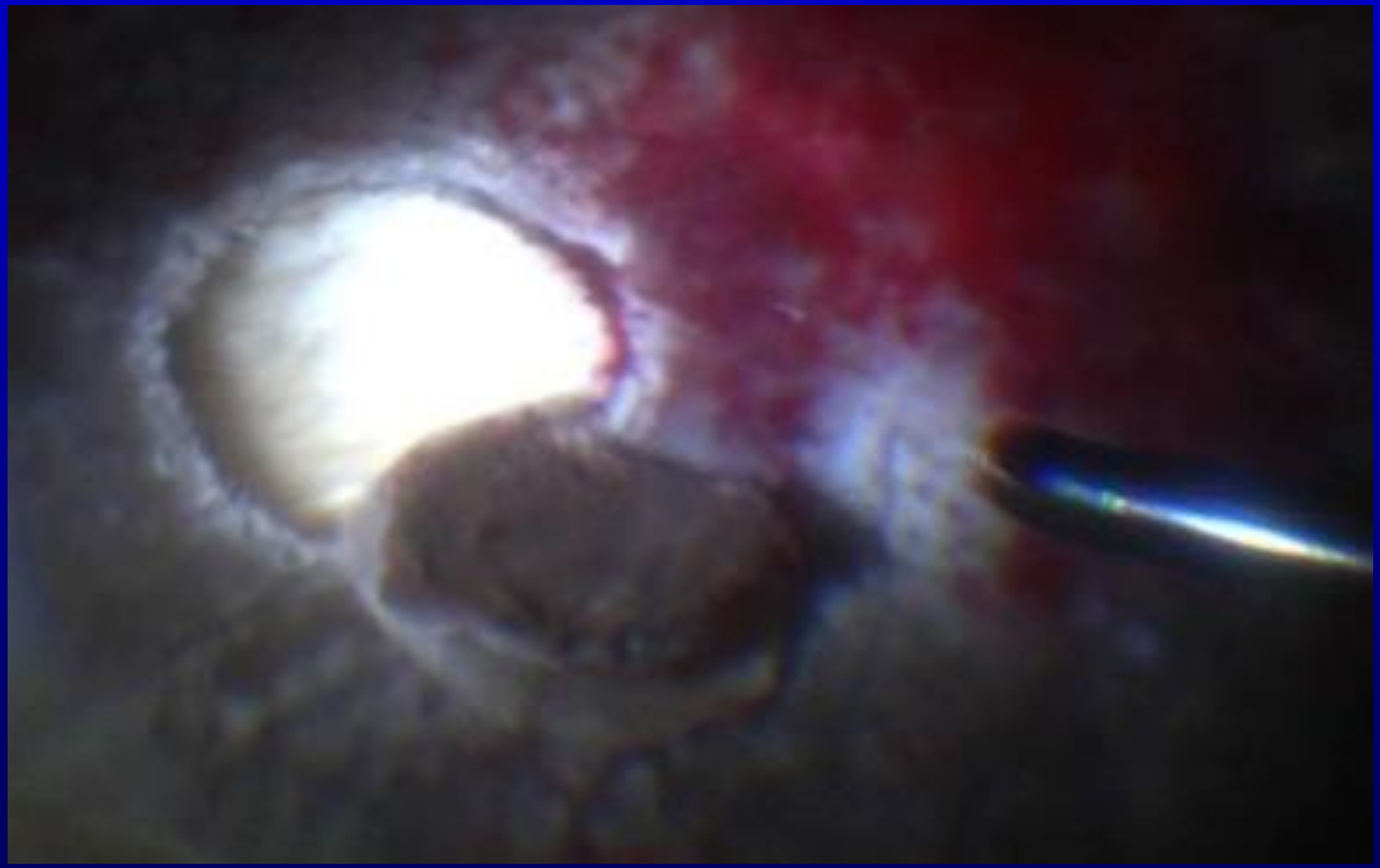


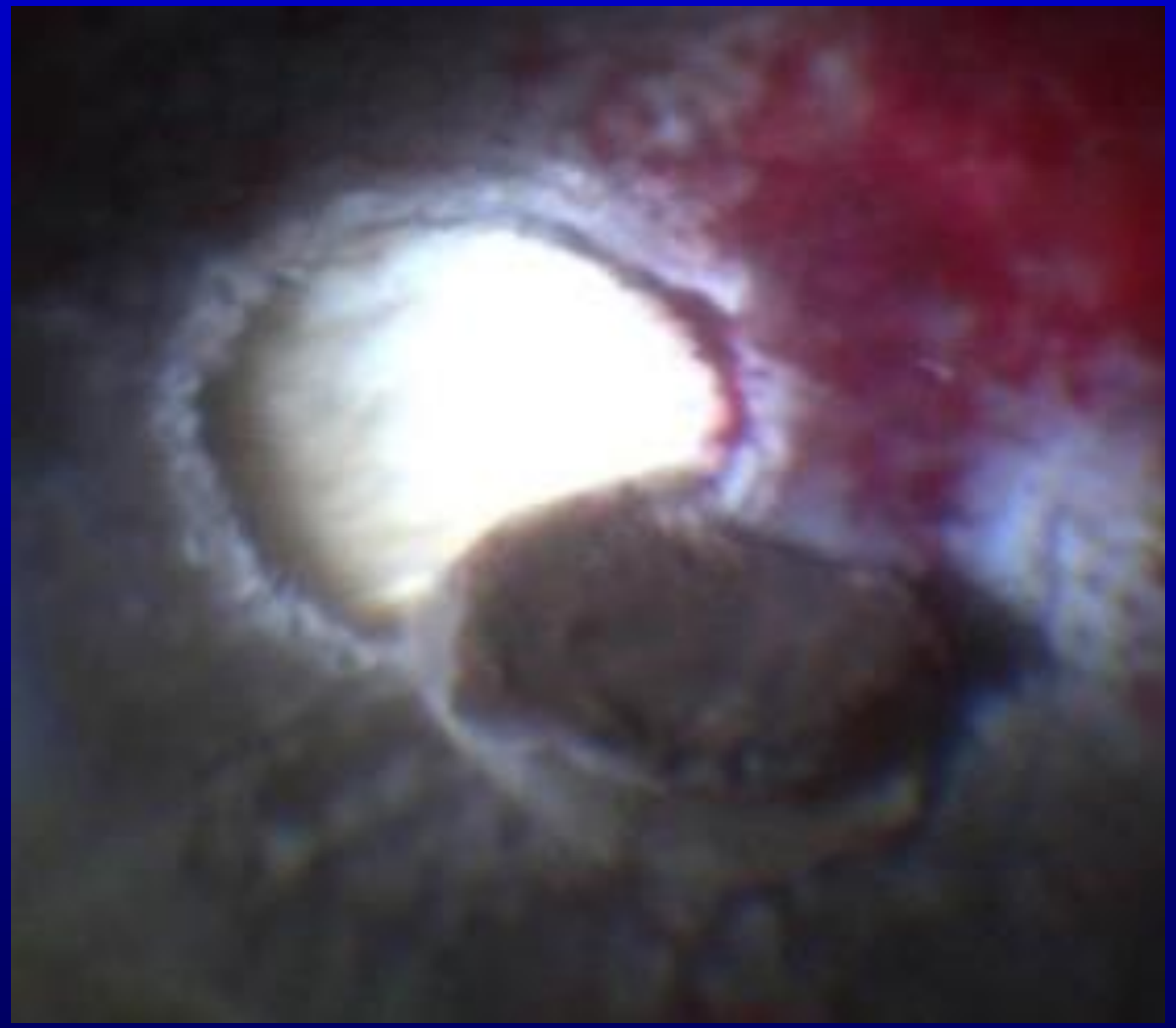
There is a need for repeated injections

Chorioretinal Biopsy



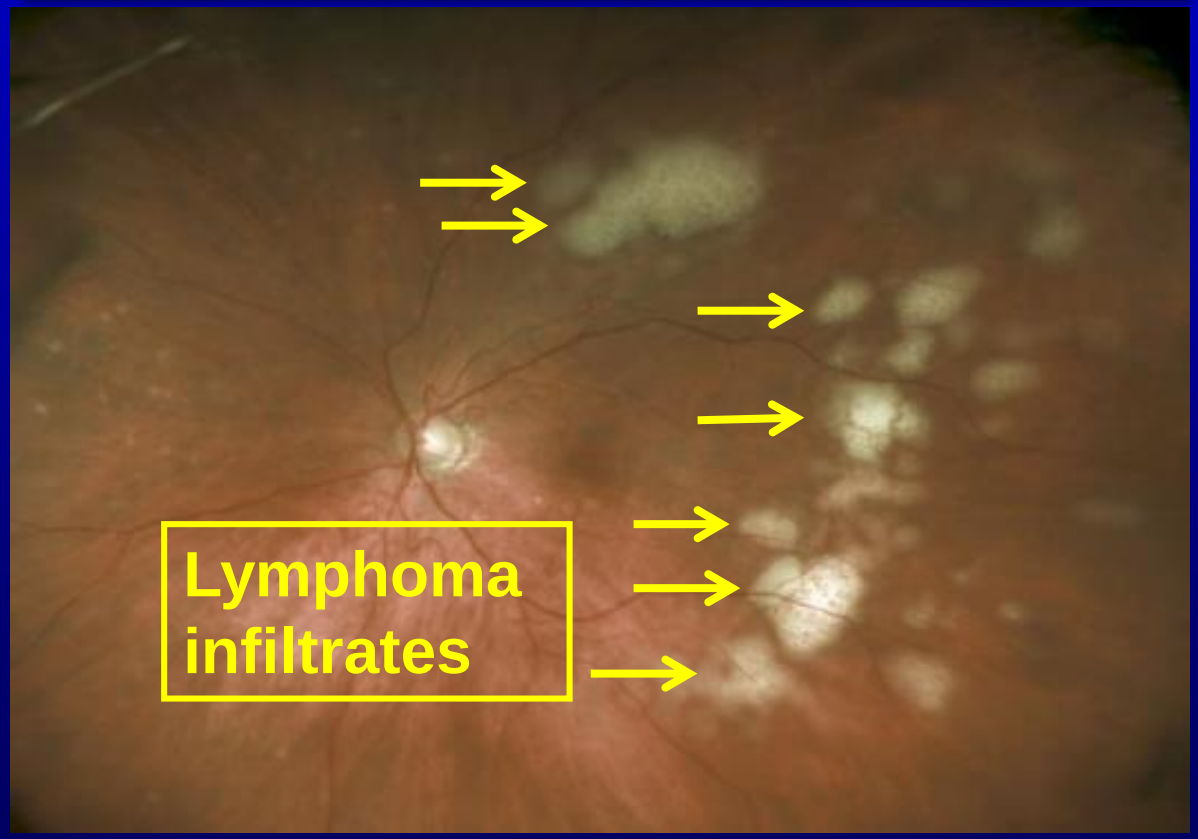
Clinical Observation

Ocular lymphoma patients who undergo chorioretinal biopsy do not develop scar tissue (epiretinal membrane or PVR) if they receive serial intravitreal methotrexate injections

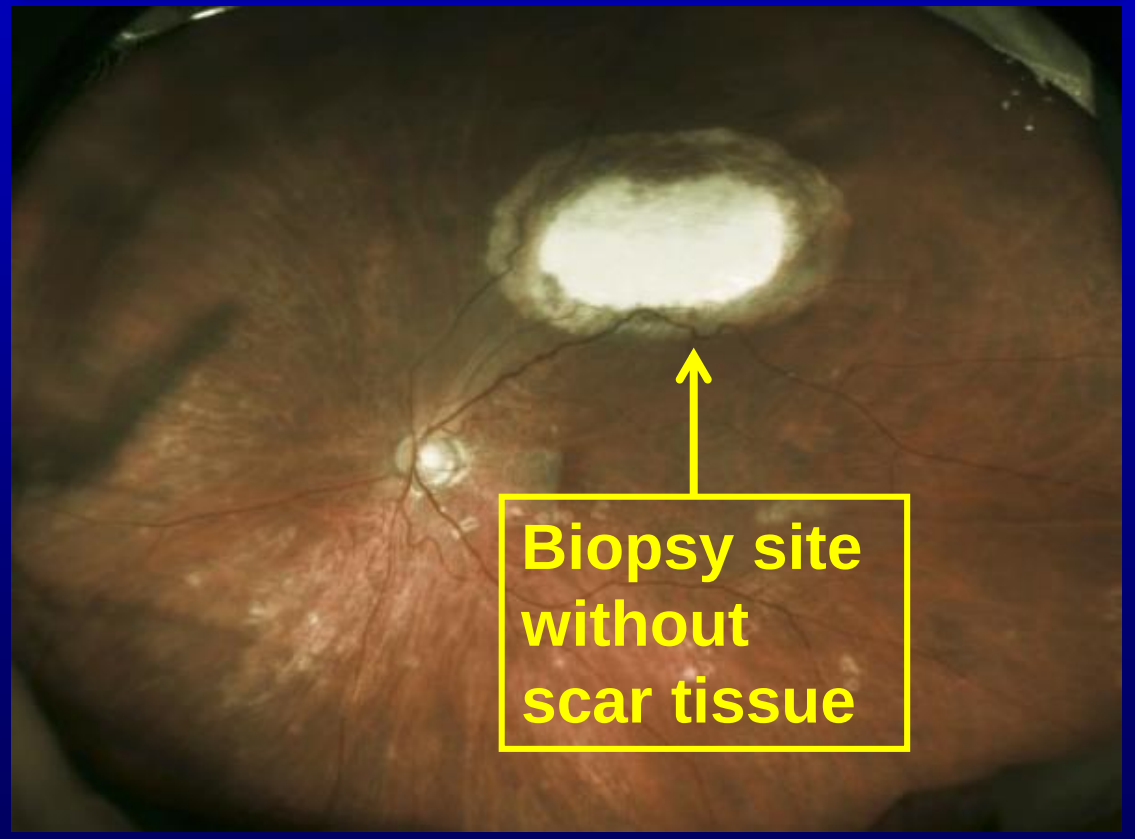


Chorioretinal Biopsy

Lymphoma, Pre-treatment

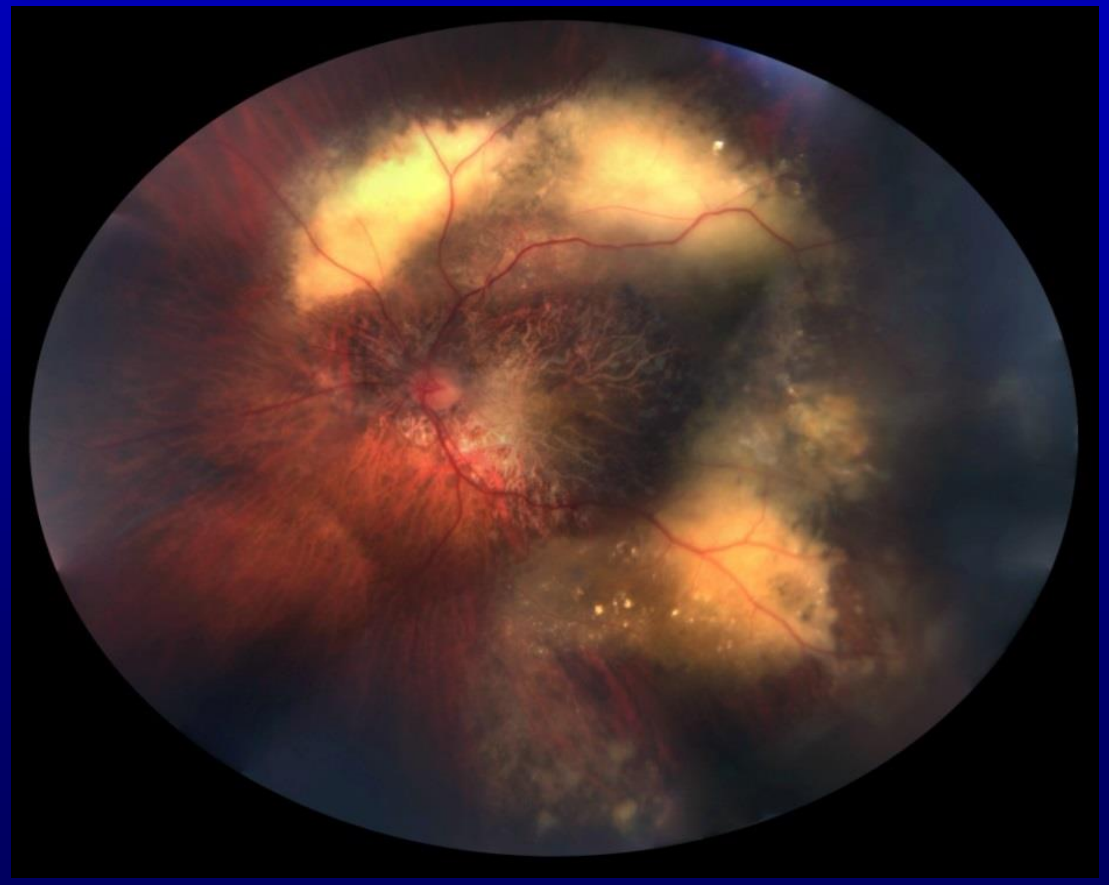


Lymphoma, Post-treatment

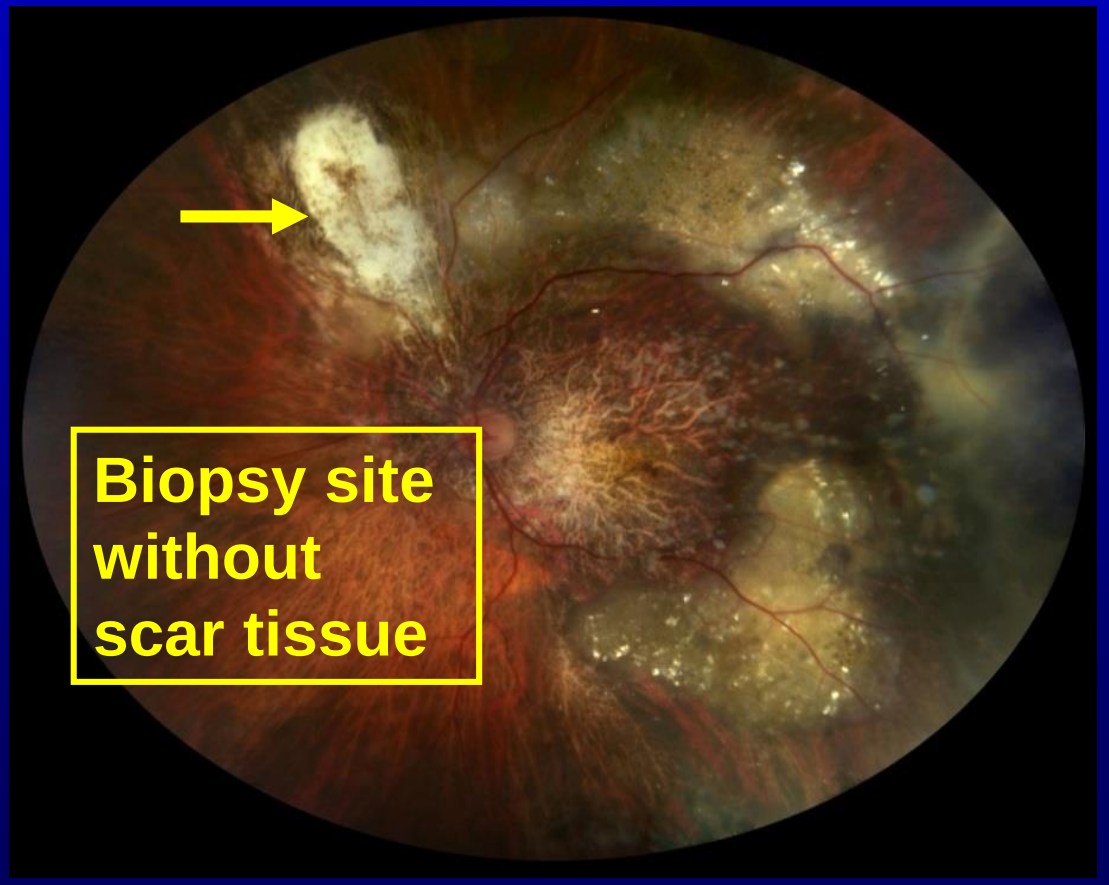


Chorioretinal Biopsy

Lymphoma, Pre-treatment



Lymphoma, Post-treatment



Chorioretinal Biopsy

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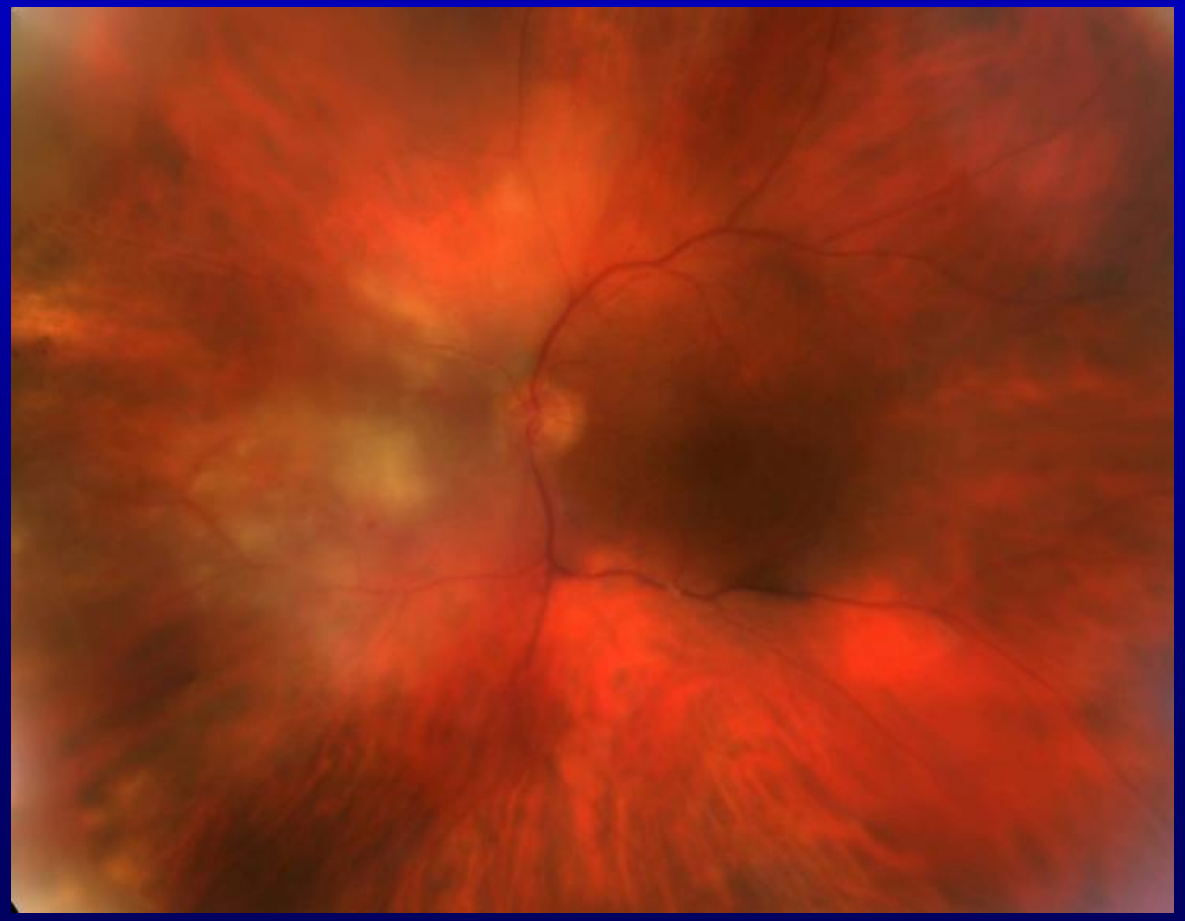
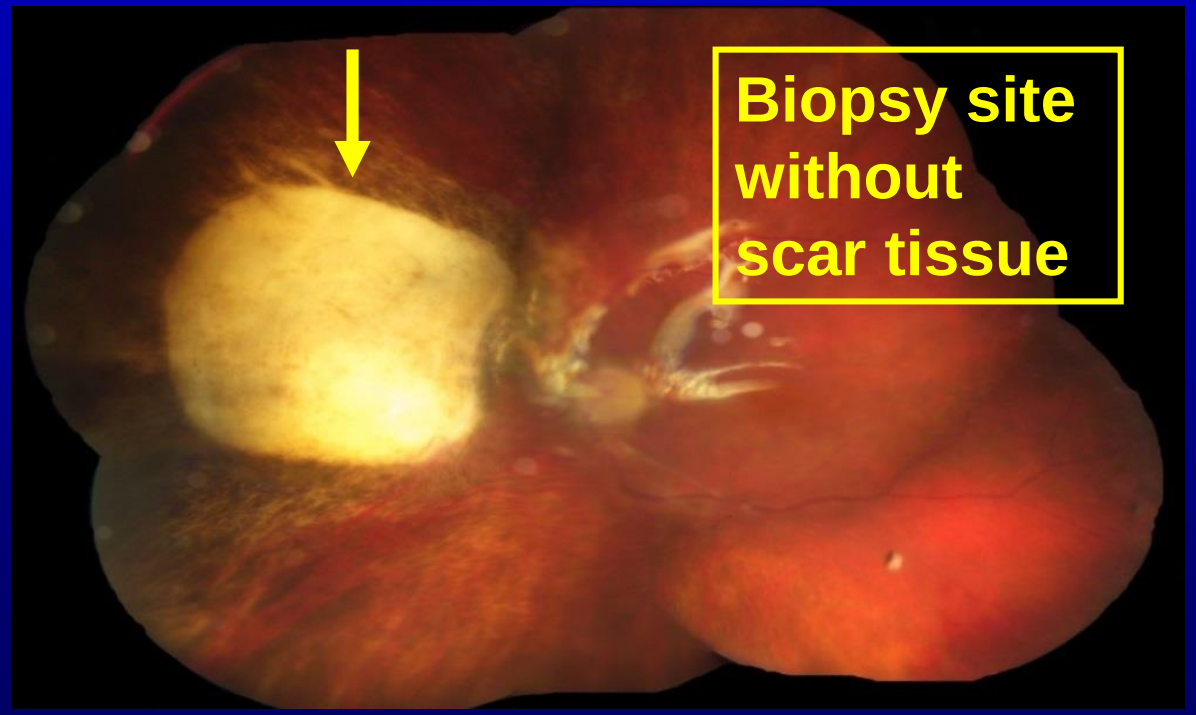
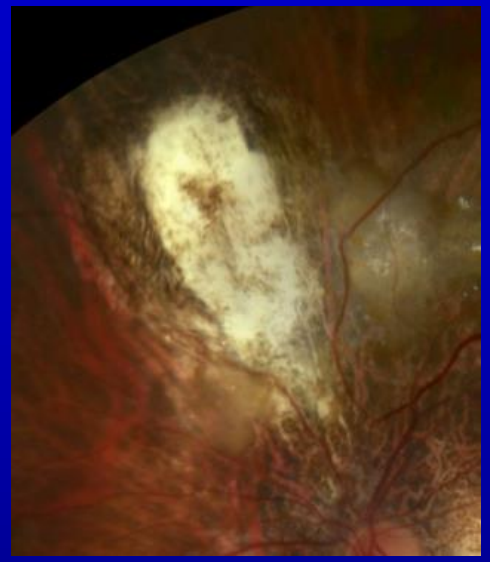
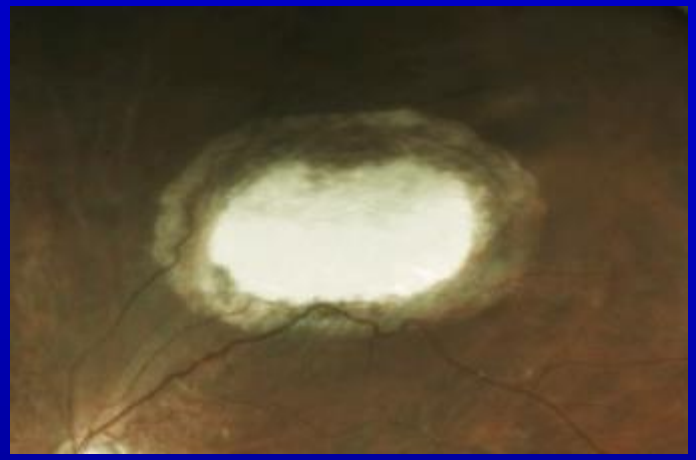


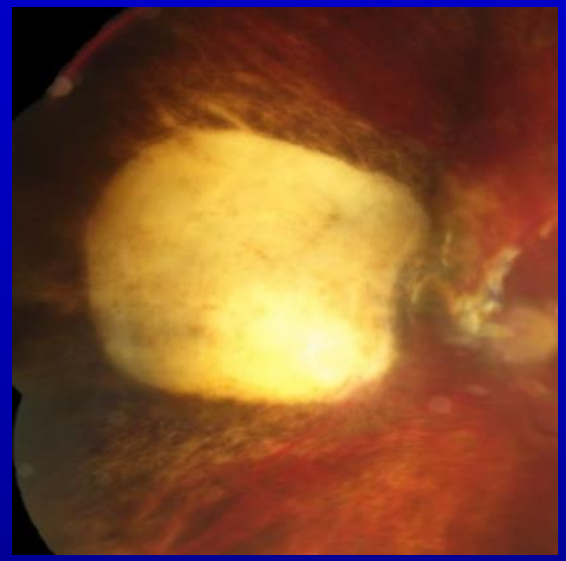
Lymphoma, Post-treatment



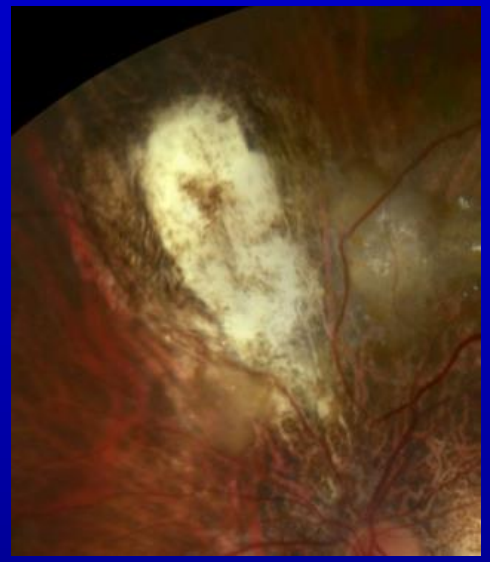
Chorioretinal Biopsy

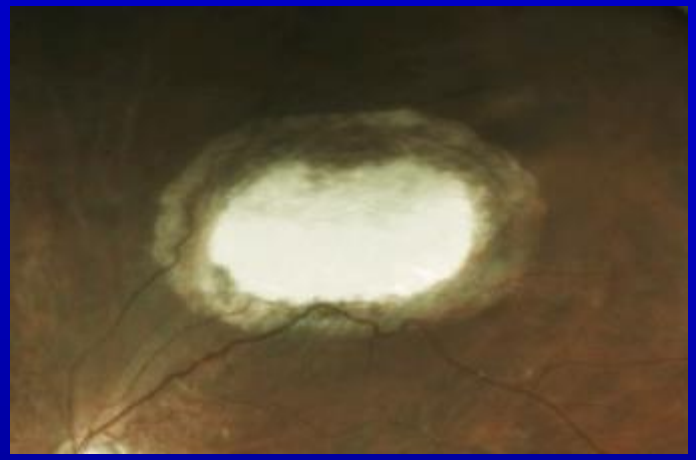


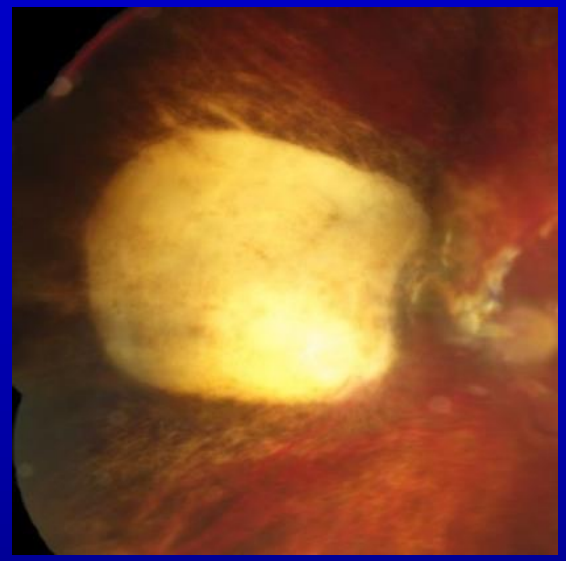




Chorioretinal Biopsy

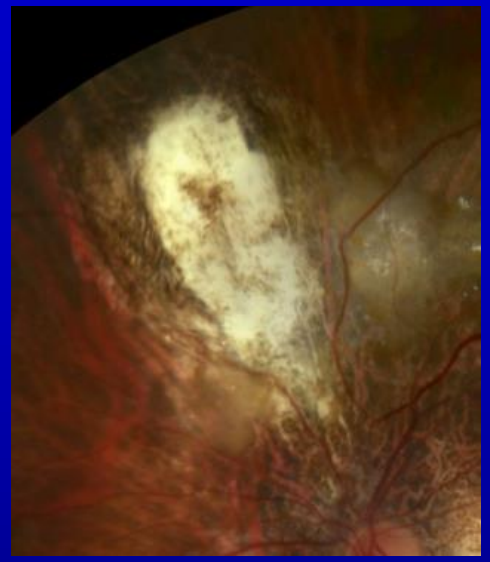


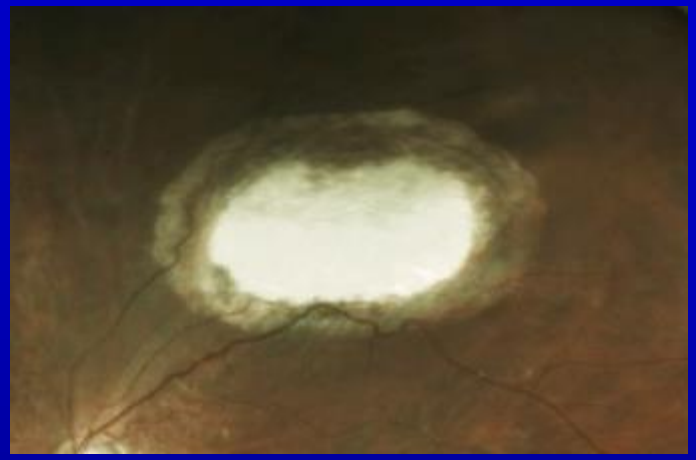


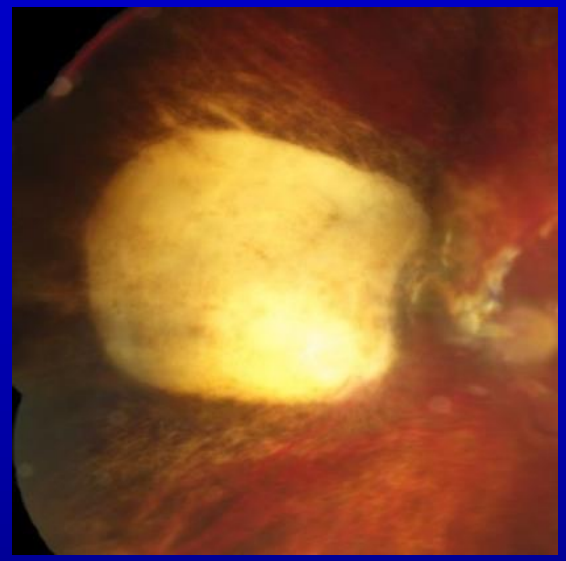


What accounts for this finding?

Chorioretinal Biopsy



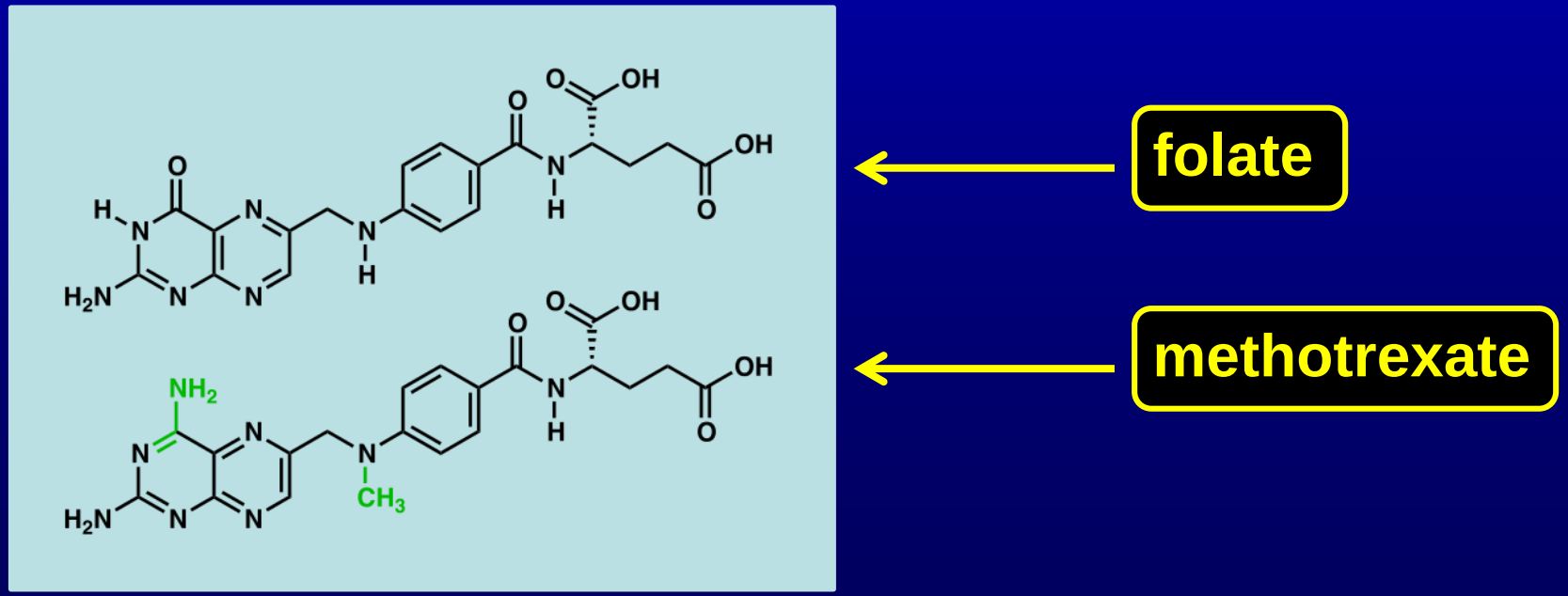




Methotrexate?

Methotrexate

- chemotherapeutic agent
  - inhibits dihydrofolate reductase
    - folate essential in thymidine systhesis



Methotrexate

- chemotherapeutic agent
  - inhibits dihydrofolate reductase
    - folate essential in thymidine systhesis

approved for a variety of cancers

Methotrexate

- chemotherapeutic agent
  - inhibits dihydrofolate reductase
    - folate essential in thymidine systhesis

multiple routes of administration

low systemic toxicity

Methotrexate

- antiinflammatory agent

Methotrexate

- antiinflammatory agent
  - different mechanism of action
    - inhibits T cell activation
    - selective down-regulation of B cells
    - binds IL-1 beta

Methotrexate

- antiinflammatory agent
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    - selective down-regulation of B cells
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approved for rheumatoid arthritis

PVR pathway

Inflammation

- blood-ocular barrier breakdown

Growth factors

- bFGF, PDGF

Cellular proliferation

- RPE, glia, macrophages, fibroblasts

Membrane contraction

- extracellular matrix / collagen

Good candidate for PVR

antiinflammatory
antiproliferative

Inflammation

- blood-ocular barrier breakdown

Growth factors

- bFGF, PDGF

Cellular proliferation

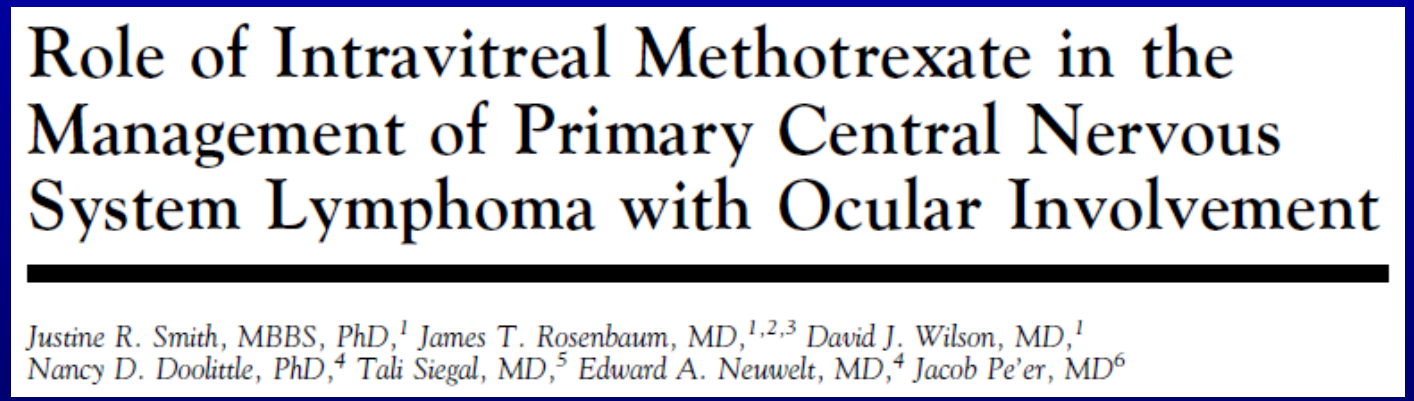
- RPE, glia, macrophages, fibroblasts

Membrane contraction

- extracellular matrix / collagen

Methotrexate

- used intravitreally for vitreoretinal lymphoma
  - low ocular toxicity, despite repeated injections



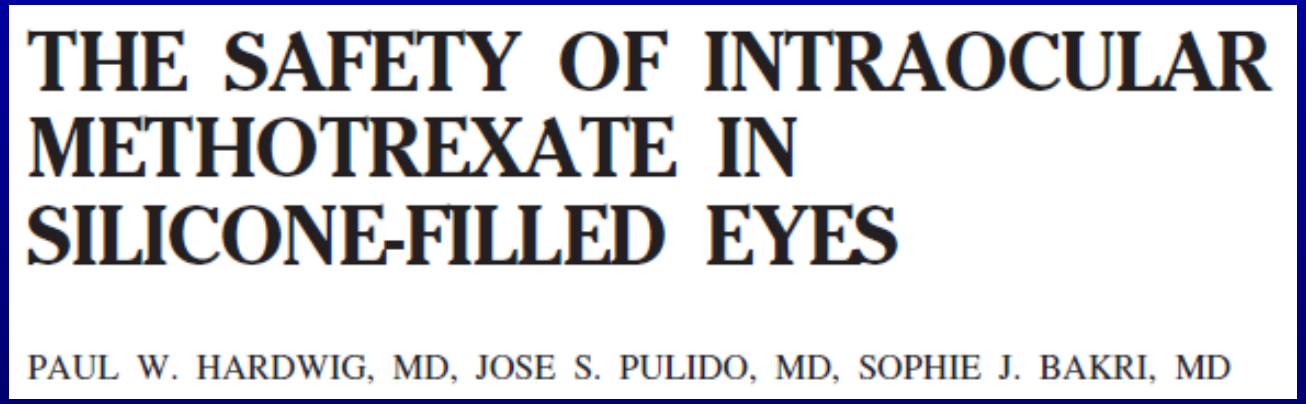
Role of Intravitreal Methotrexate in the Management of Primary Central Nervous System Lymphoma with Ocular Involvement

Justine R. Smith, MBBS, PhD,[1] James T. Rosenbaum, MD,[1,2,3] David J. Wilson, MD,[1]
Nancy D. Doolittle, PhD,[4] Tali Siegal, MD,[5] Edward A. Neuwelt, MD,[4] Jacob Pe'er, MD[6]

Ophthalmology 109:1709-1716,2002

Methotrexate

- used intravitreally for vitreoretinal lymphoma
  - evidence of safety in oil



THE SAFETY OF INTRAOCULAR METHOTREXATE IN SILICONE-FILLED EYES

PAUL W. HARDWIG, MD, JOSE S. PULIDO, MD, SOPHIE J. BAKRI, MD

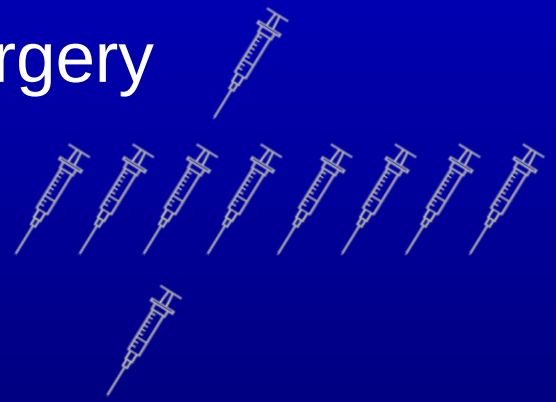
Retina 28:1082-1086,2008

Phase 1 Study

- 10 patients
  - prospective study
  - IND from FDA
  - IRB approval

Phase 1 Study

- 10 patients
  - prospective study
  - IND from FDA
  - IRB approval
- 10 injections over 3 month period
  - 1 at end of surgery
  - weekly x 8
  - 1 at 3 months



Phase 1 Study

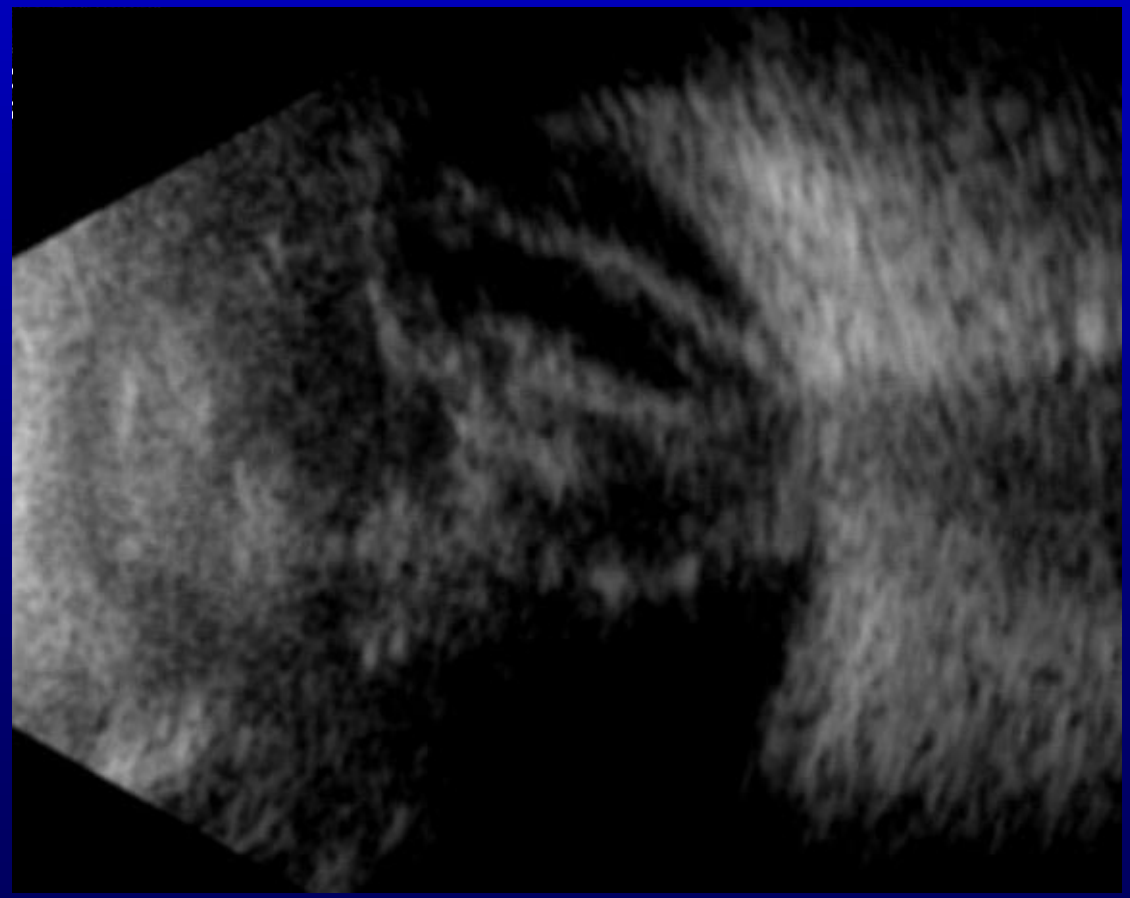
- 10 patients
  - 2 severe trauma with retinal incarceration in scleral wound
  - 8 recurrent retinal detachment / PVR
    - multiple prior surgeries
  - median preop VA: HM

Phase 1 Study

- 10 patients
  - surgery
    - all underwent extensive retinectomy
    - all had silicone oil
  - protocol
    - 99% compliance (99 out of 100 injections)

Phase 1 Study

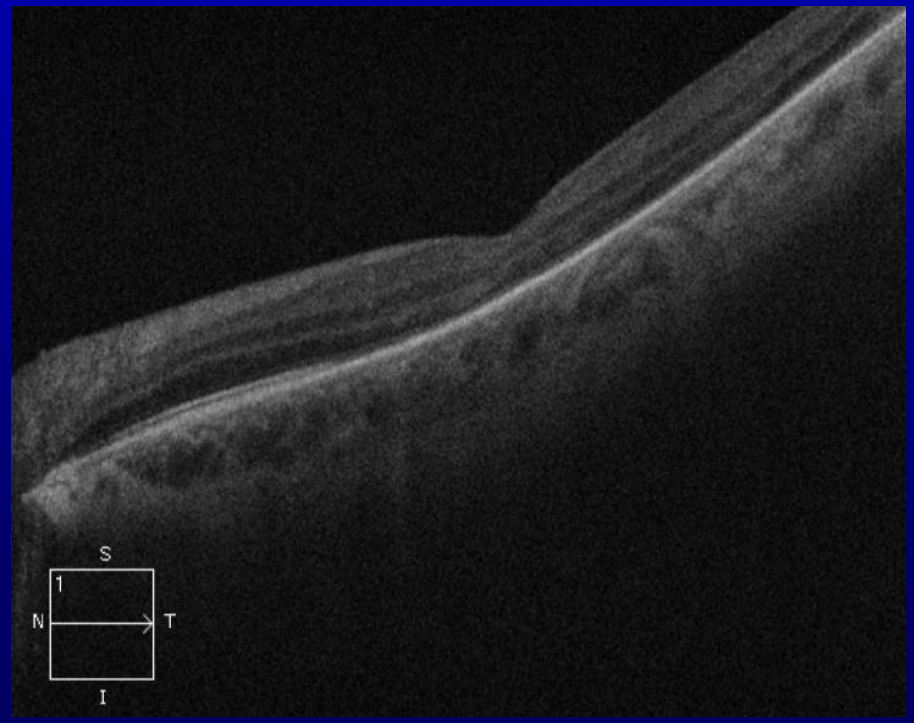
- Trauma patient #1
  - 37 mm scleral rupture, zone 3
    - retina incarcerated in scleral wound



Ultrasound showing total retinal detachment

Phase 1 Study

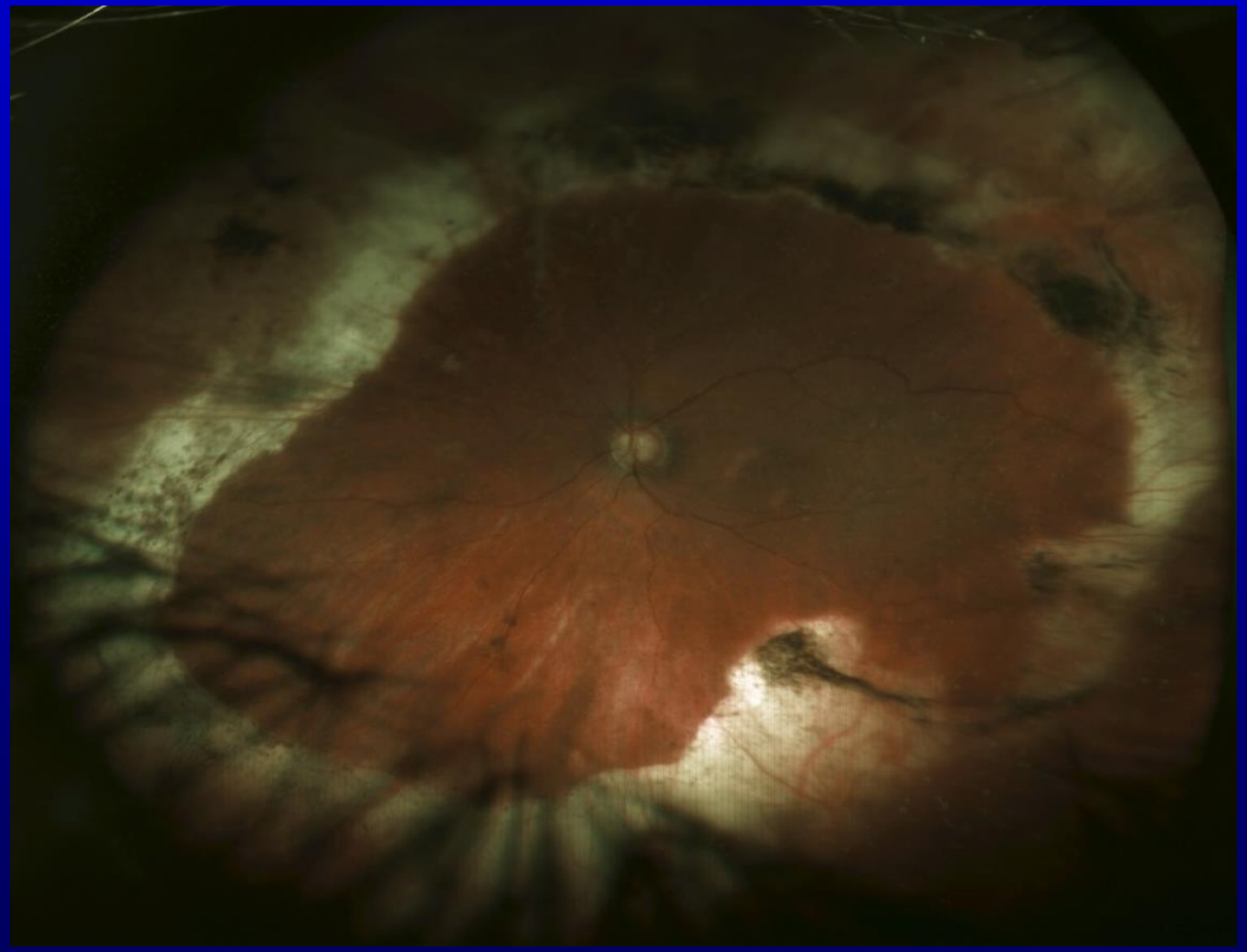
- Trauma patient #1
  - postop month 4



Phase 1 Study

- Trauma patient #1
  - postop year 5

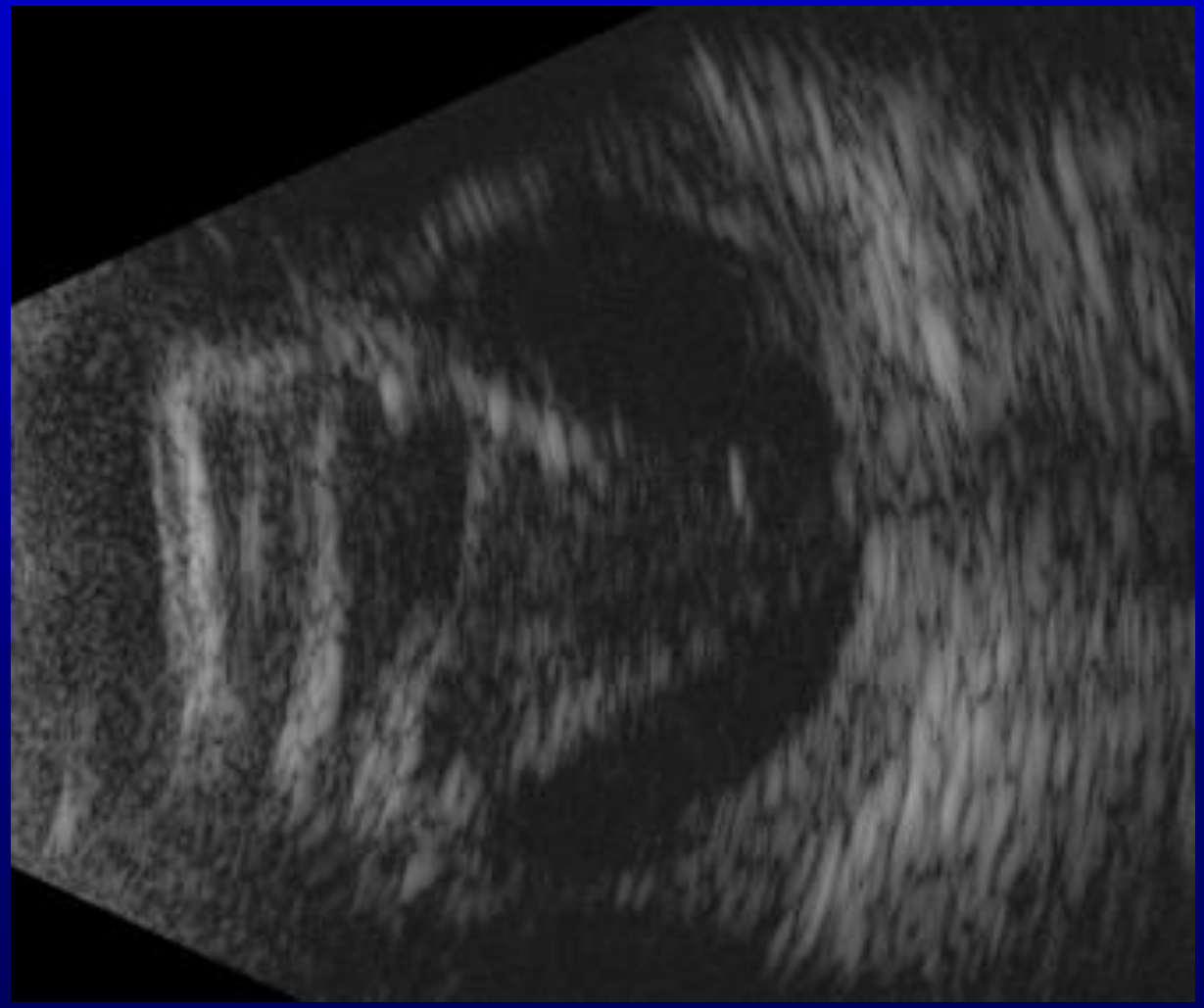
20/65



Phase 1 Study

- Trauma patient #2
  - 13 mm scleral rupture, zone 3
    - retina incarcerated in scleral wound

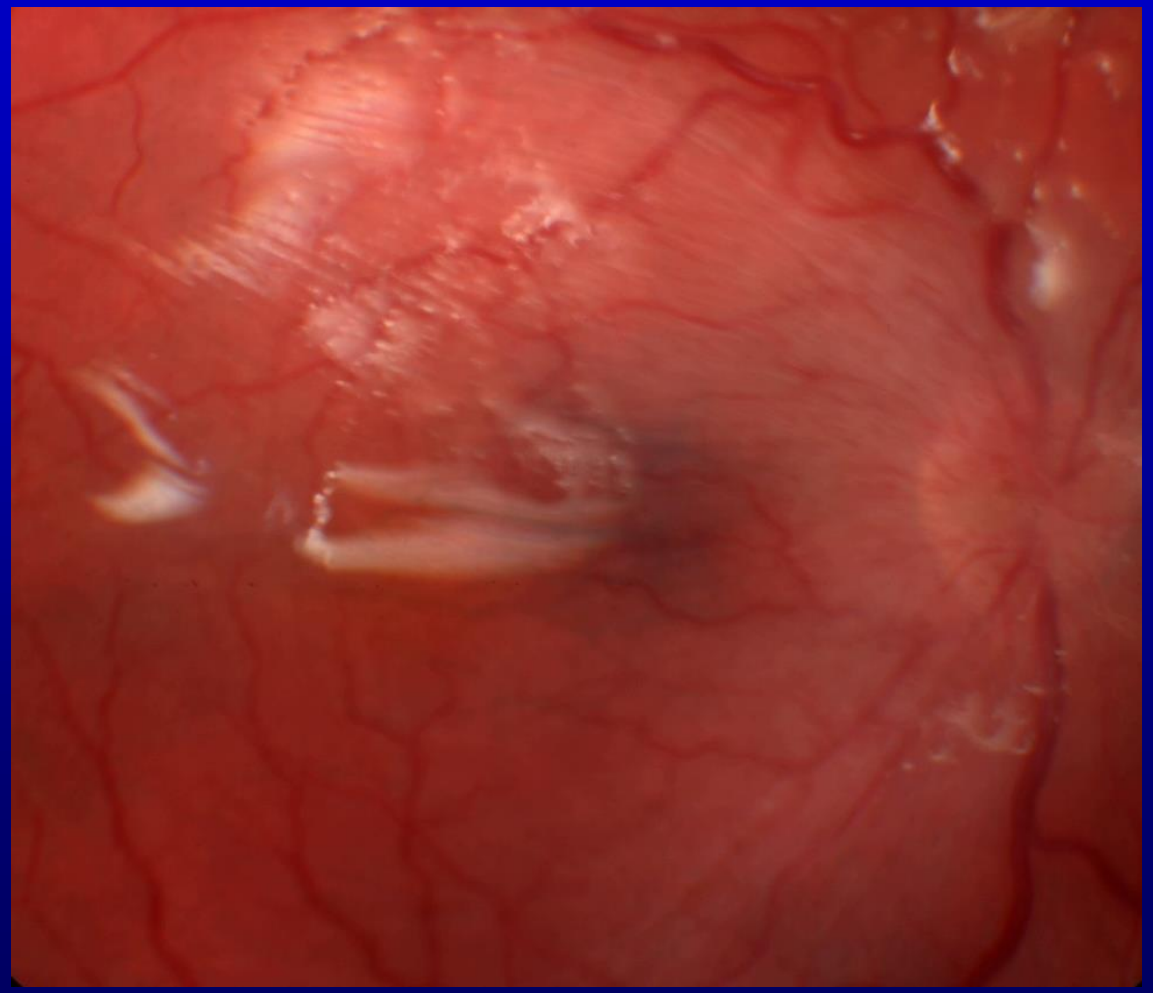
Ultrasound showing total retinal detachment



Phase 1 Study

- Trauma patient #2
  - postop week 7

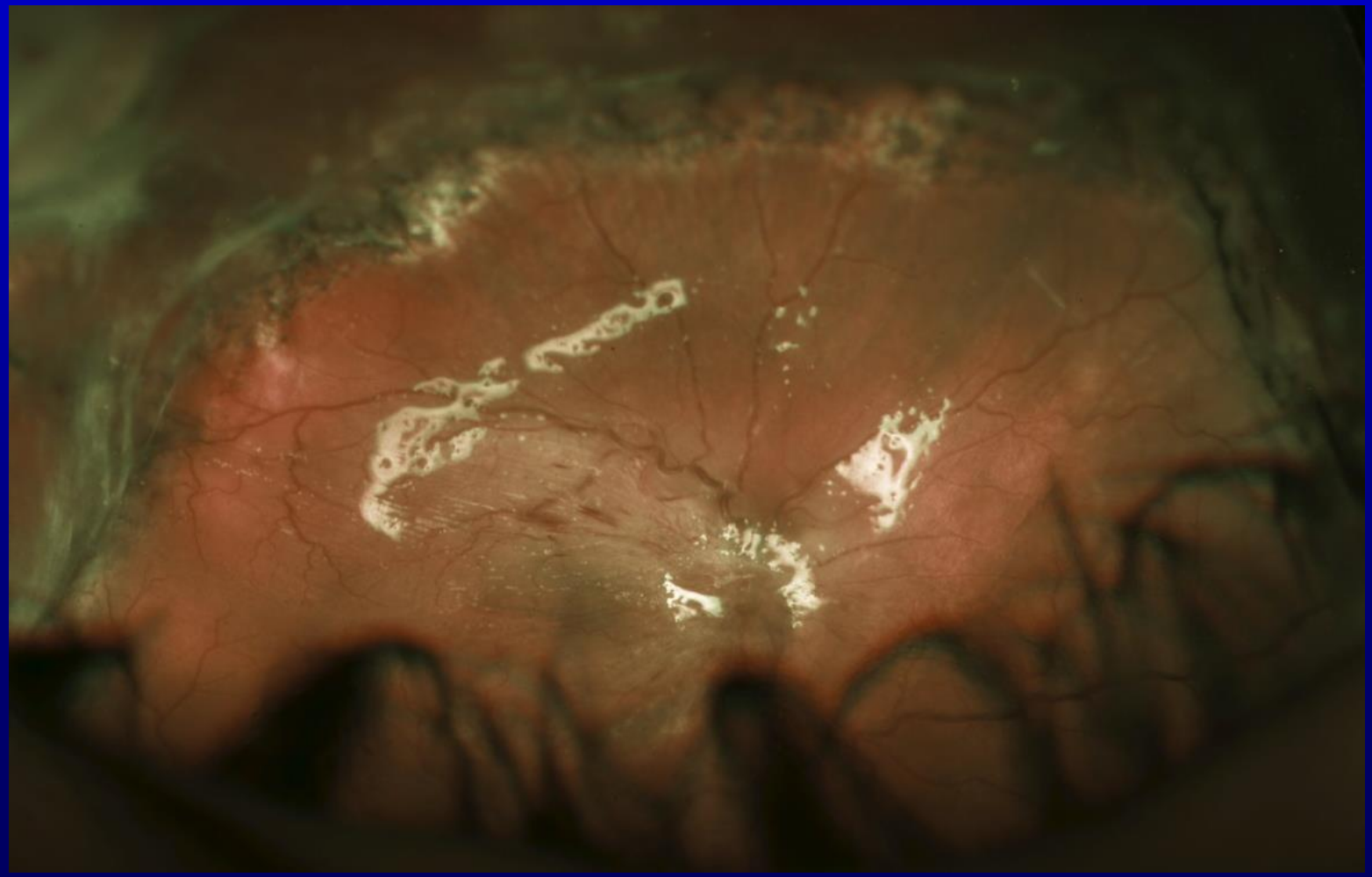
20/160



Phase 1 Study

- Trauma patient #2
  - postop week 12

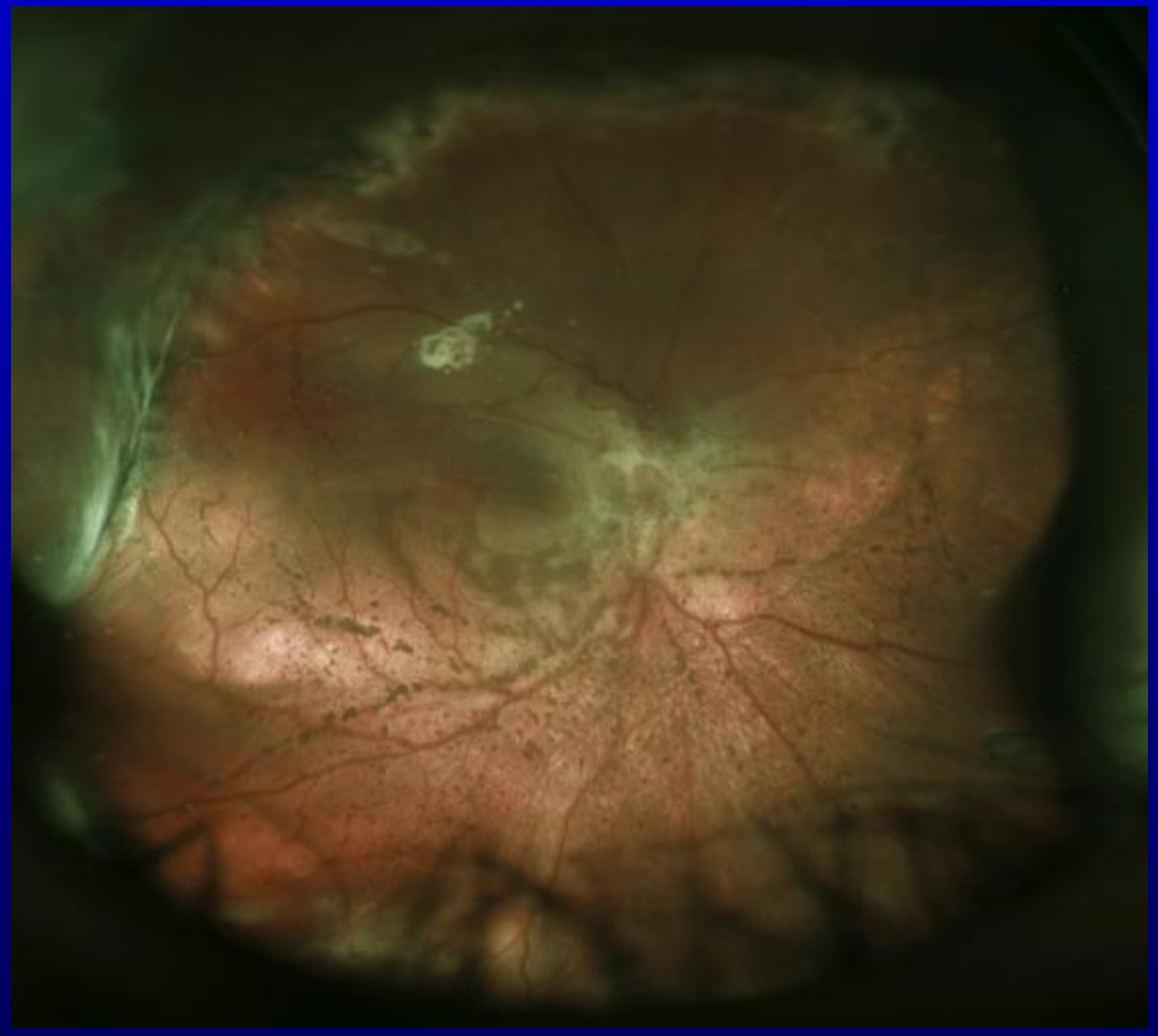
20/160



Phase 1 Study

- Trauma patient #2
  - postop week 16

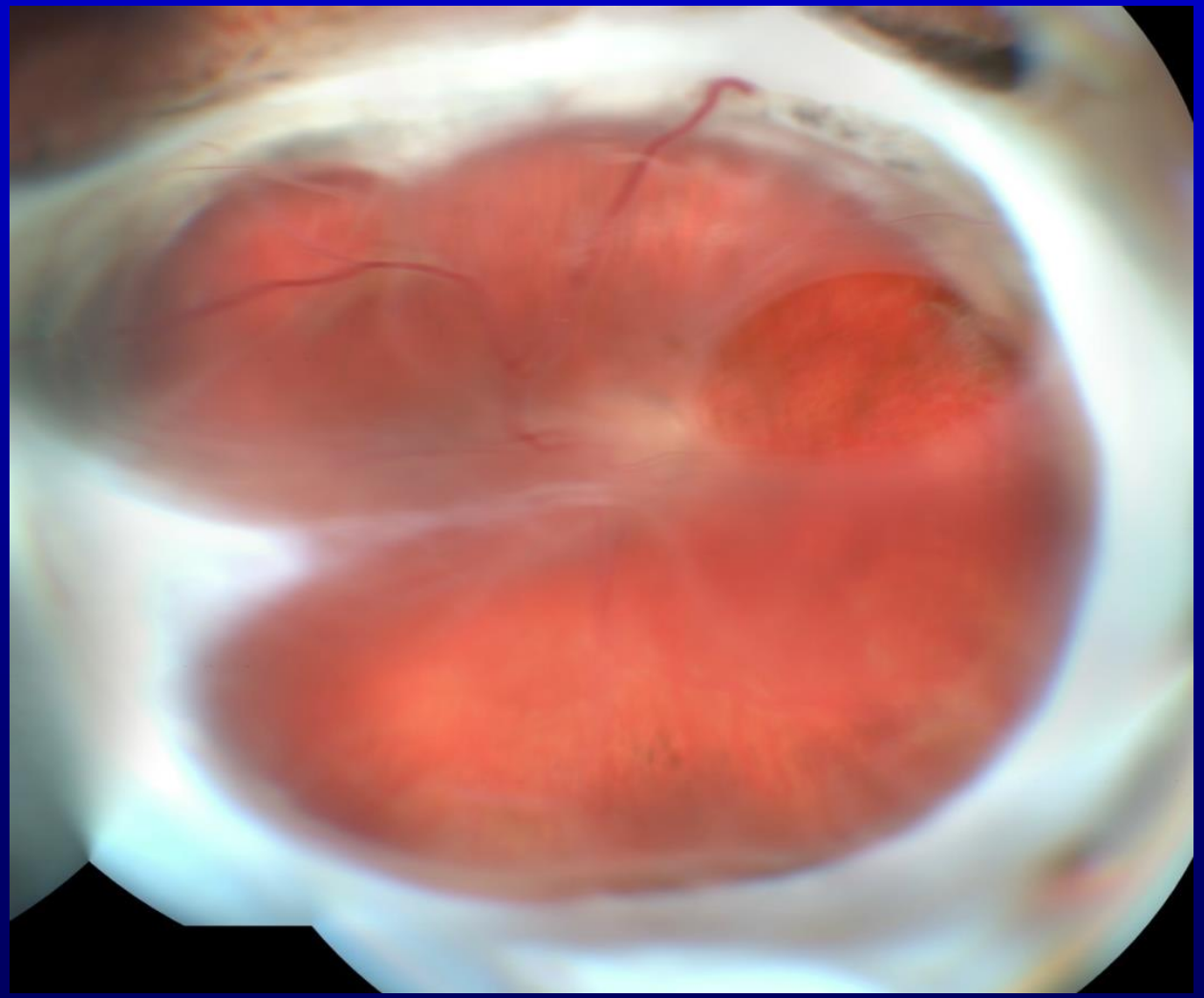
20/160



Phase 1 Study

- Trauma patient #2
  - postop year 2

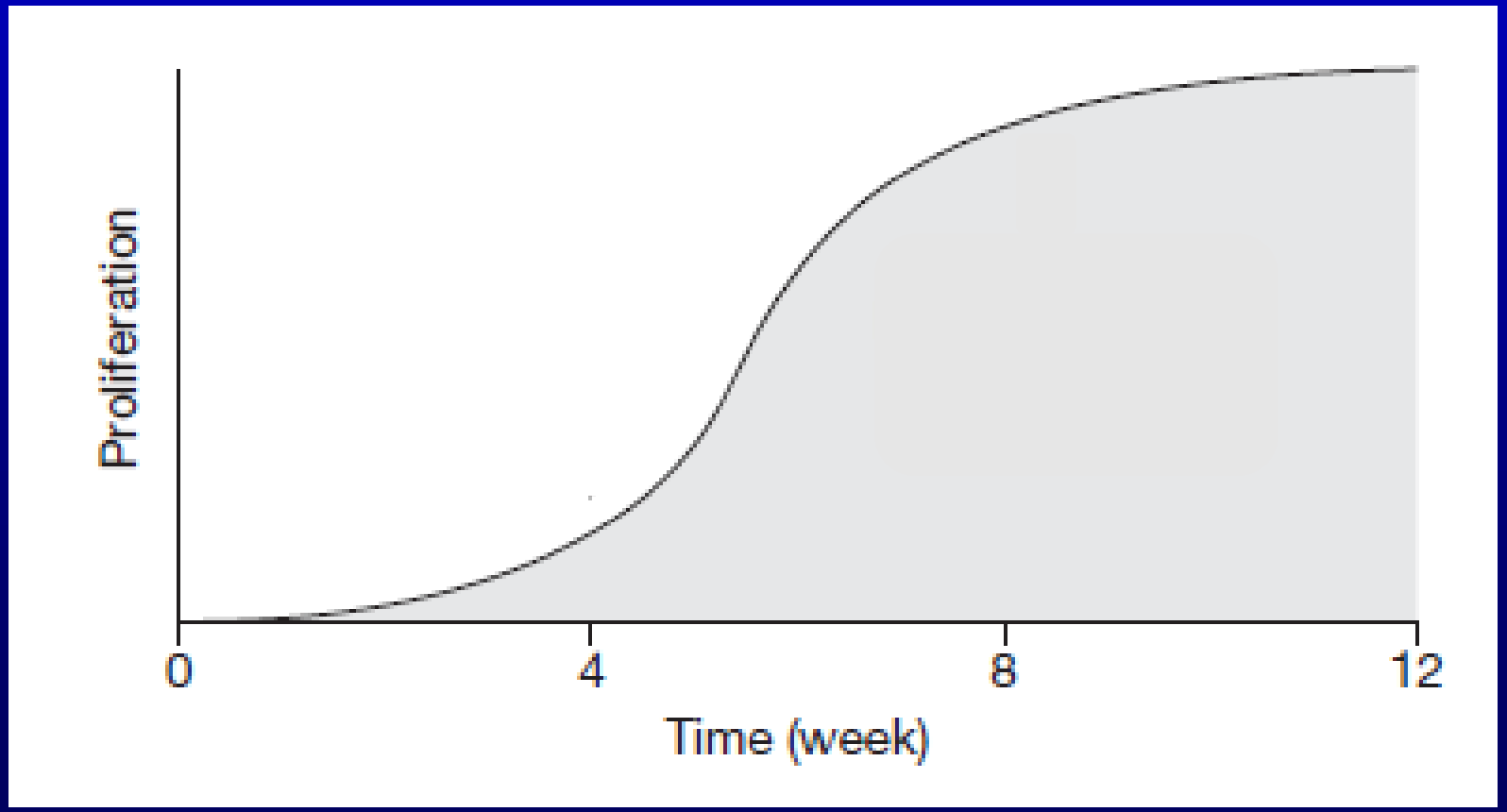
Light Perception

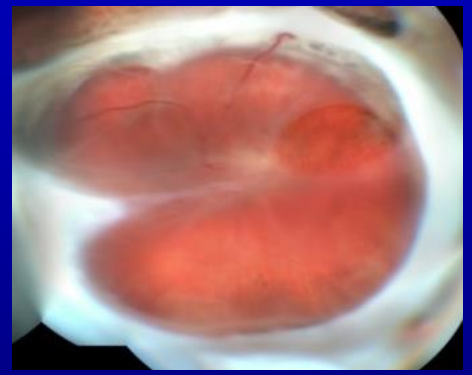


Phase 1 Study

- Trauma patient #2

no PVR → severe PVR

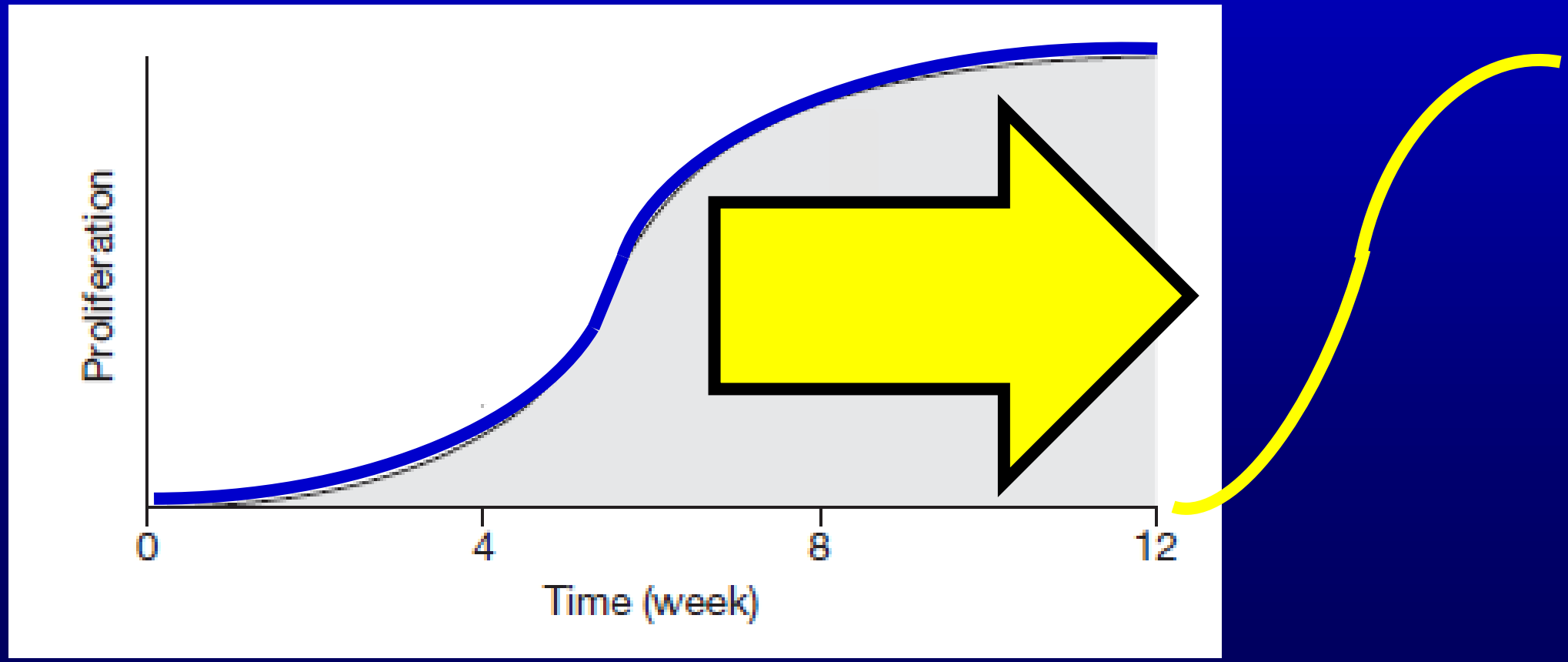




Phase 1 Study

- Trauma patient #2

no PVR → severe PVR



Phase 1 Study

- 10 patients
  - none developed hypotony
  - 3 developed subretinal fluid

Phase 1 Study

- 10 patients
  - none developed hypotony
  - 3 developed subretinal fluid
    - microscopic PVR?

Phase 1 Study

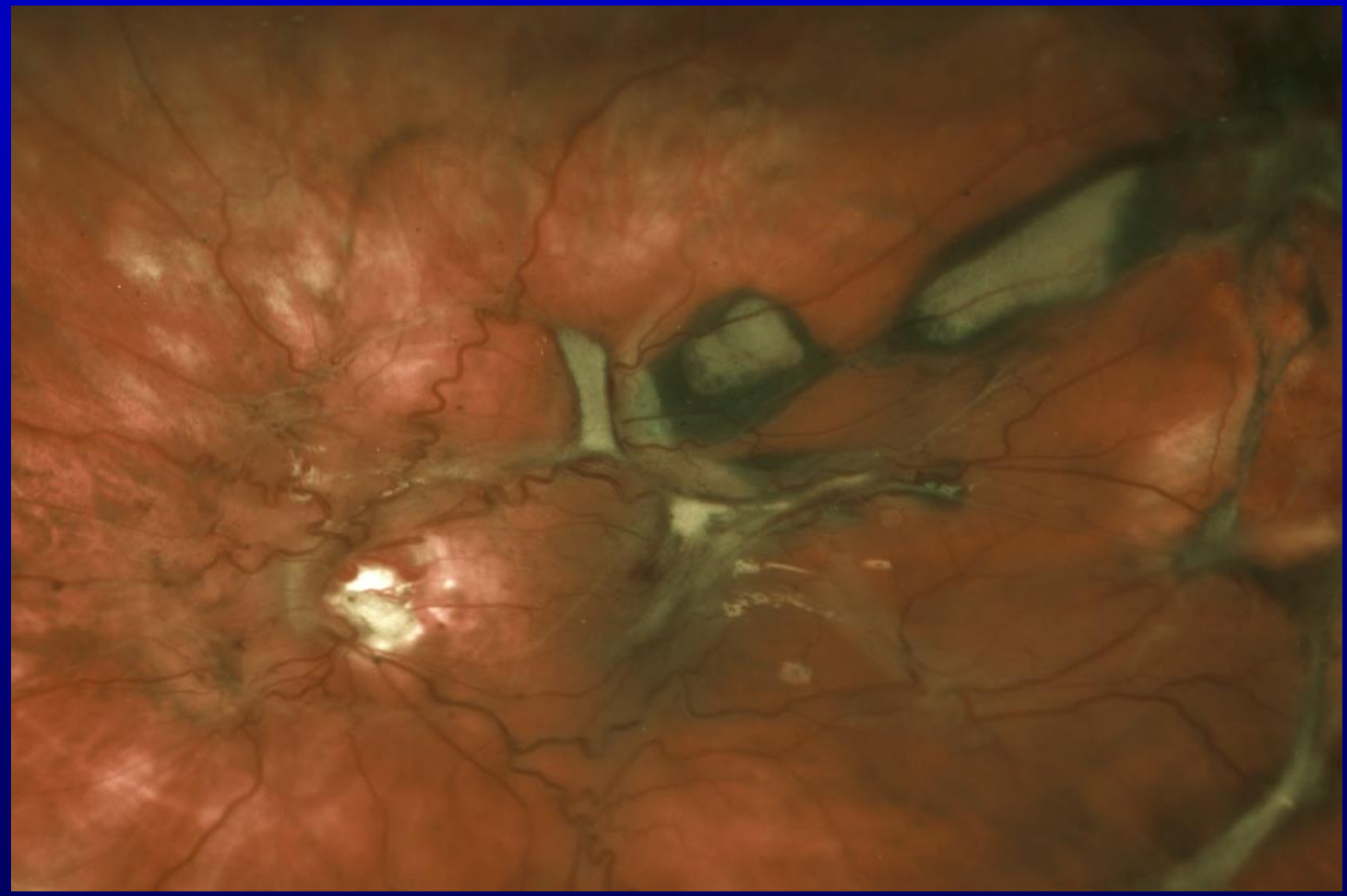
- 10 patients
  - none developed hypotony
  - 3 developed subretinal fluid
    - microscopic PVR?
    - intrinsic retinal contraction?

Phase 1 Study

- 10 patients
  - none developed hypotony
  - 3 developed subretinal fluid
    - microscopic PVR?
    - intrinsic retinal contraction?
    - inadequate laser-induced chorioretinal adhesion?

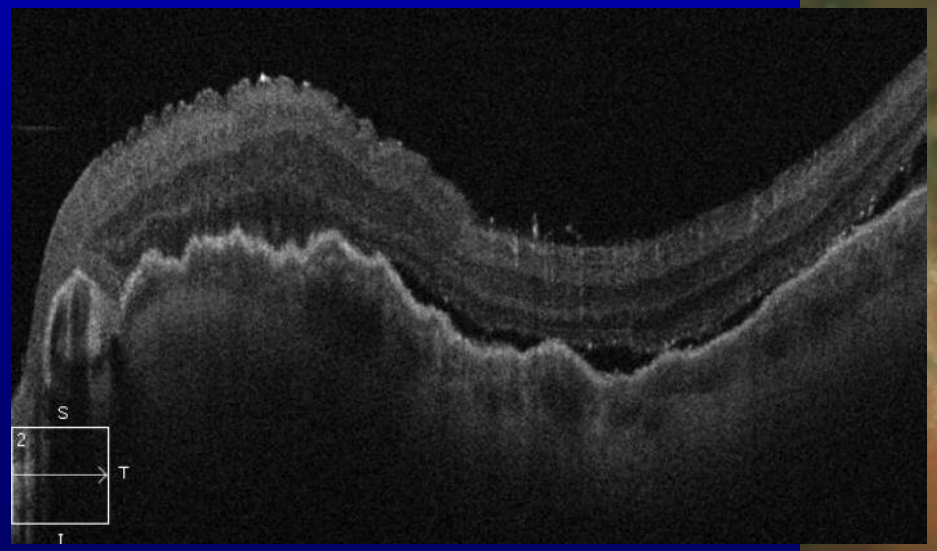
Phase 1 Study

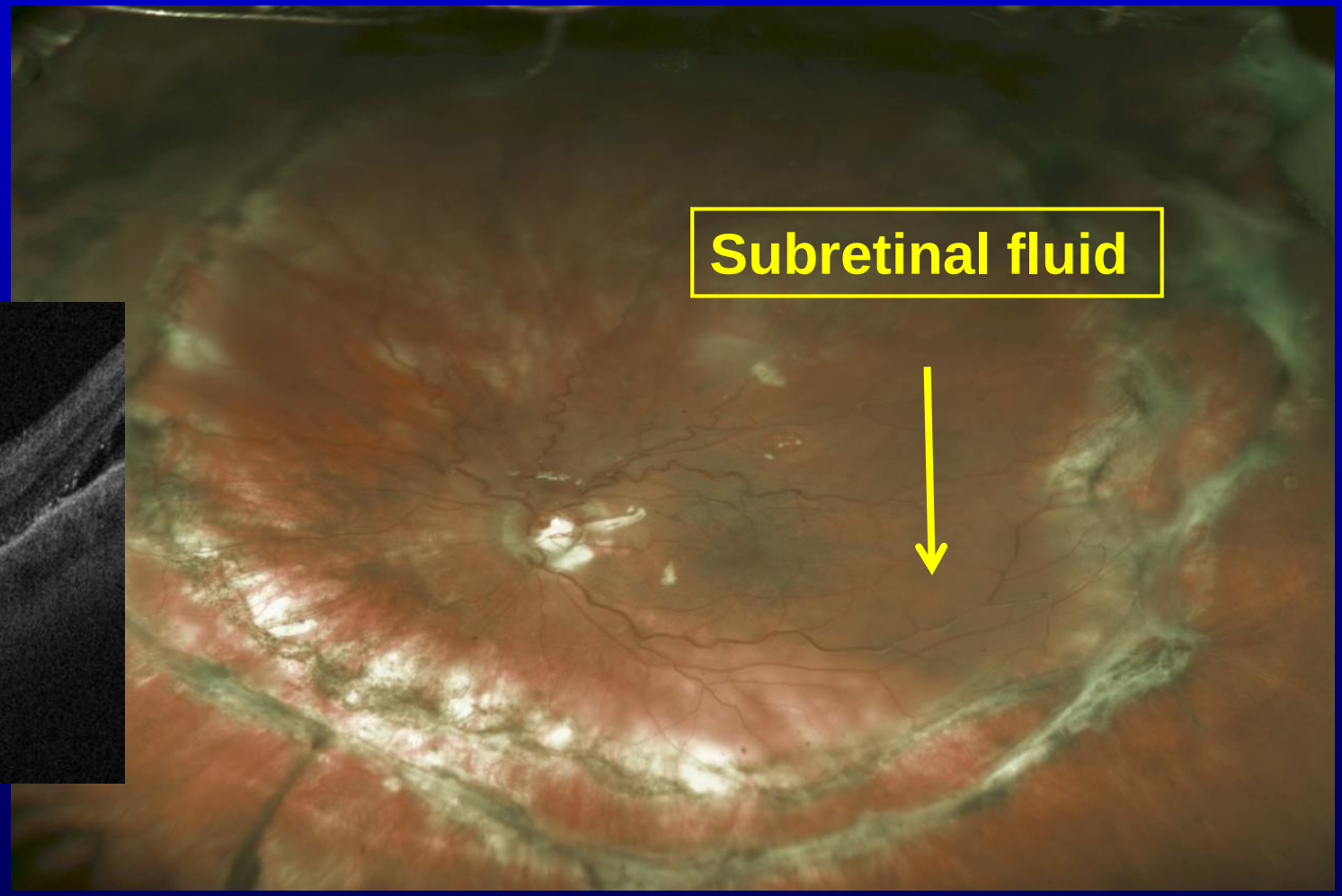
- Patient #5
  - preop



Phase 1 Study

- Patient #5
  - postop week 6

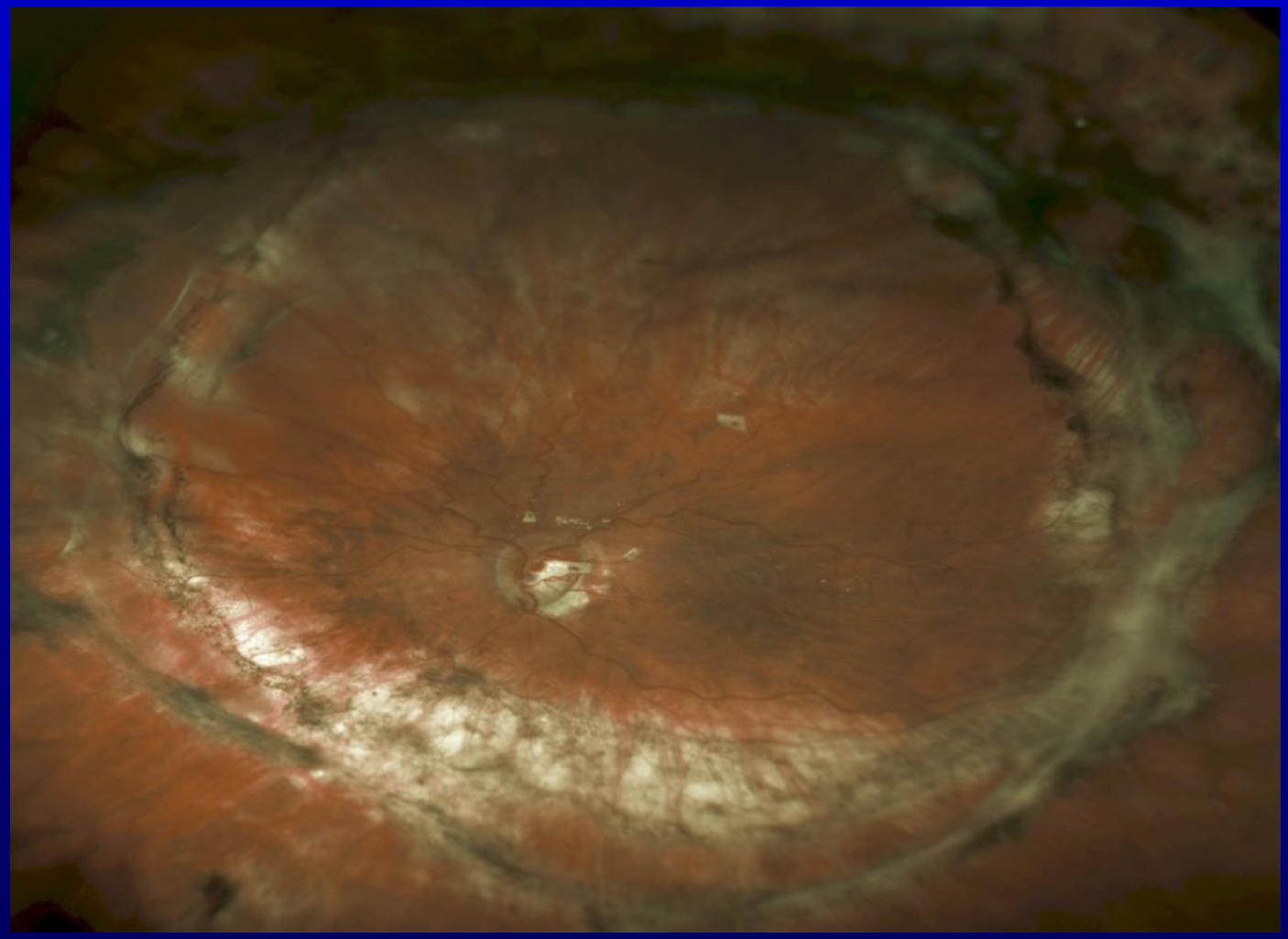




Phase 1 Study

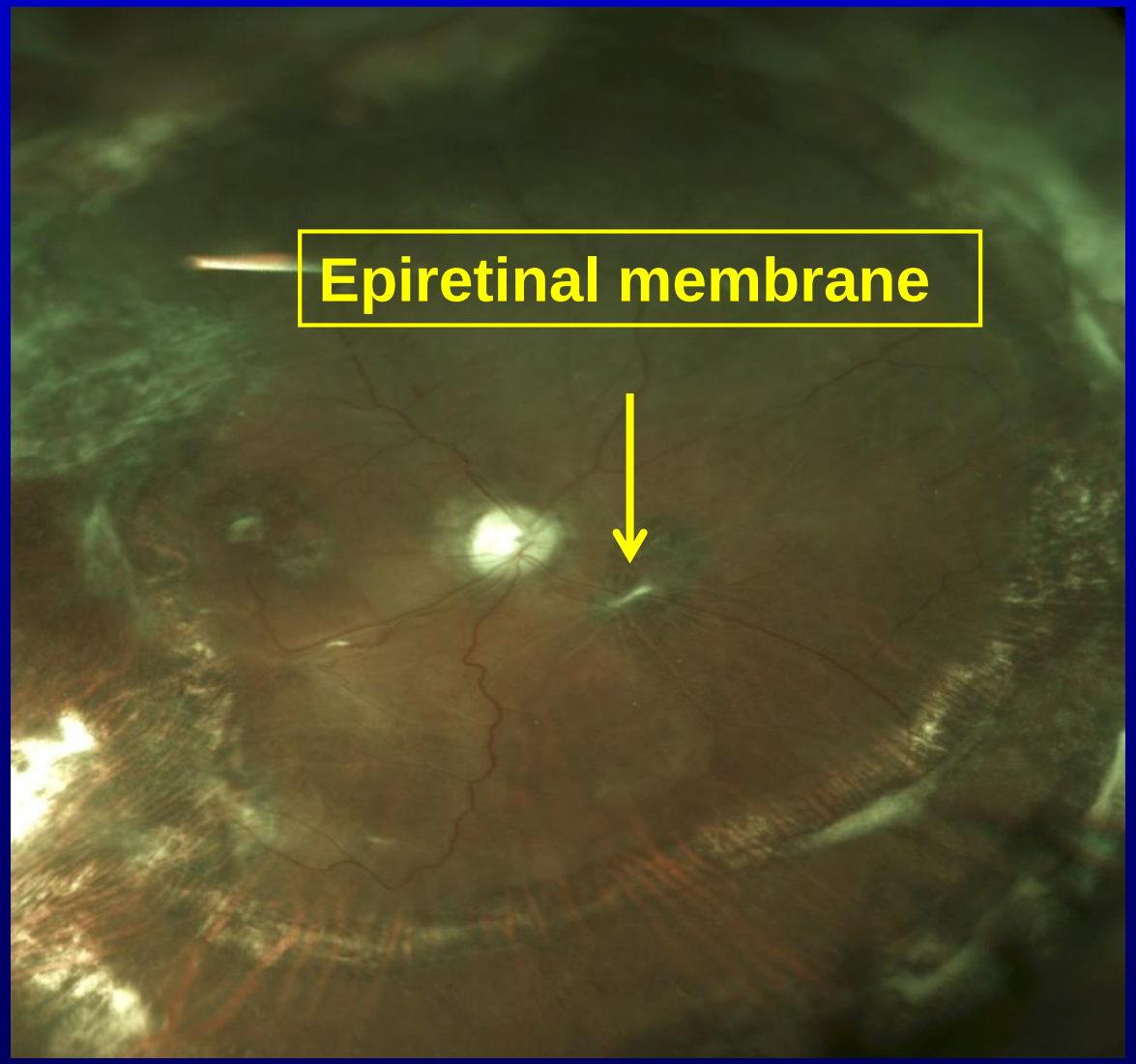
- Patient #5
  - after reoperation

20/200



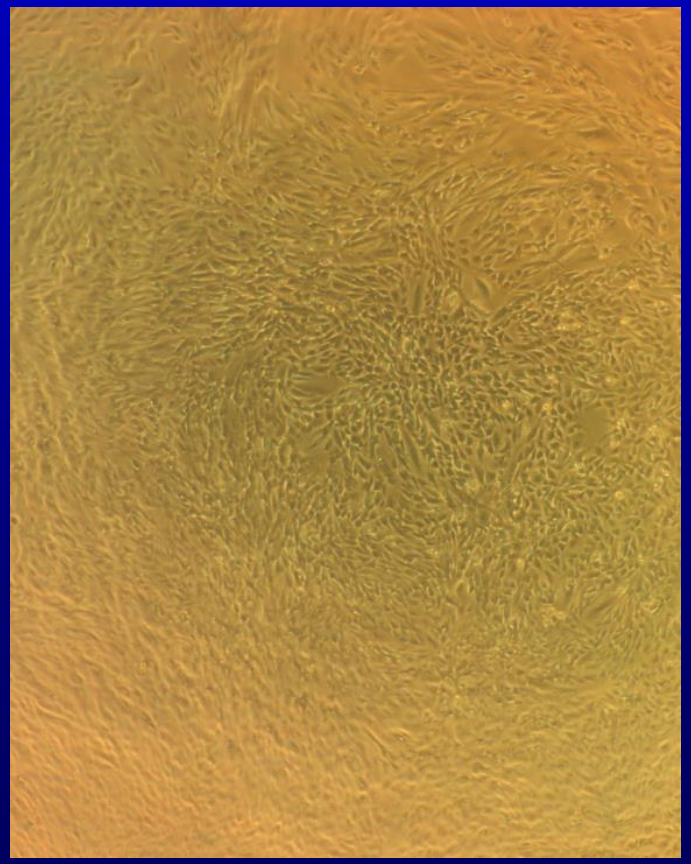
Phase 1 Study

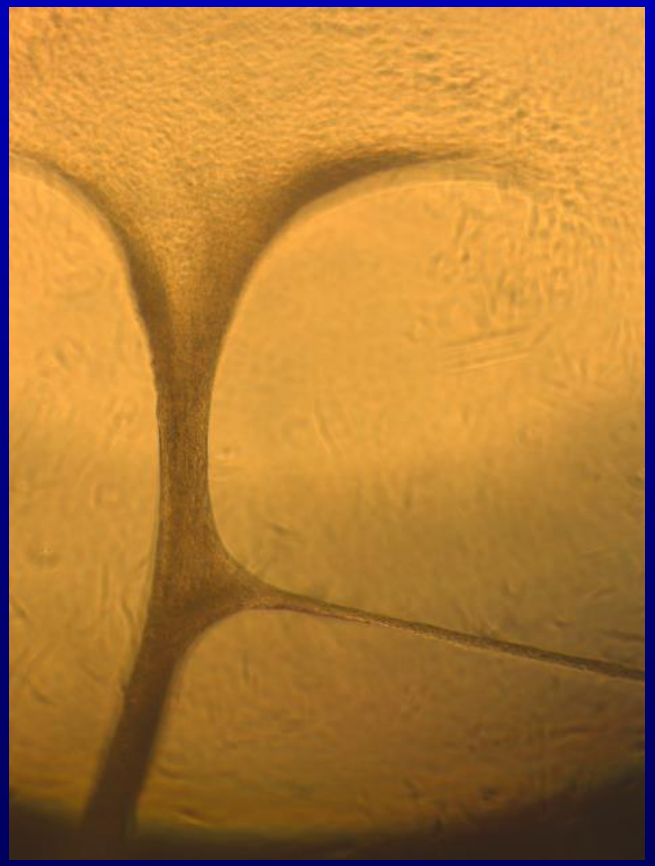
- Patient #3
  - epiretinal membrane



Lab Studies

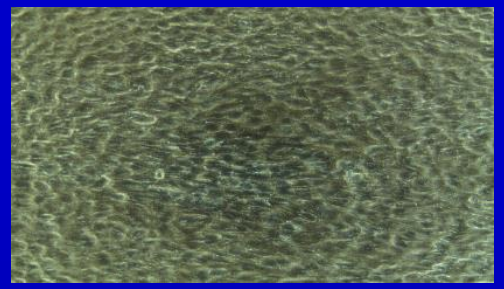
- cultures of patient membranes

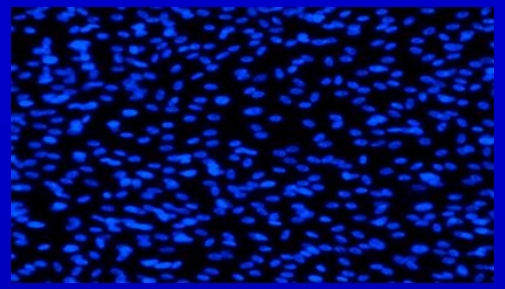




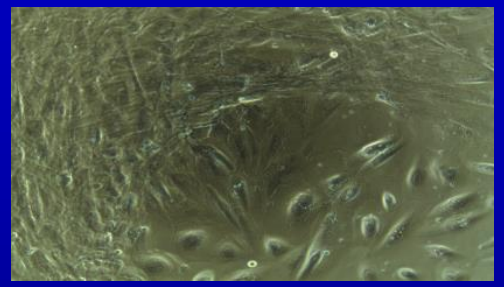
phase contrast immunofluorescence

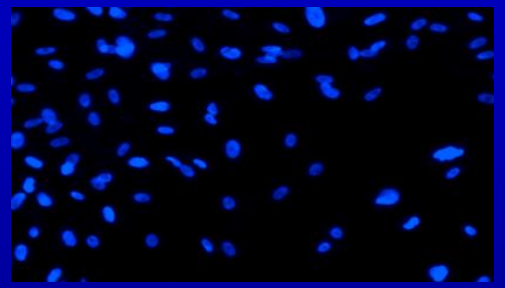
control



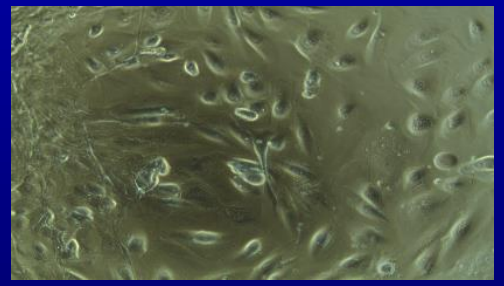


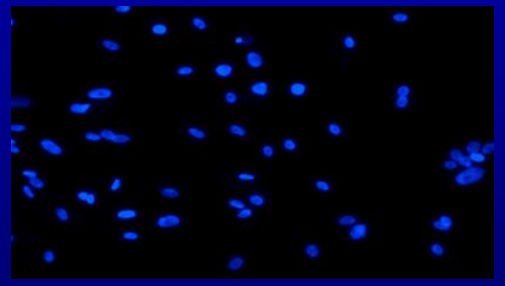
100 μM



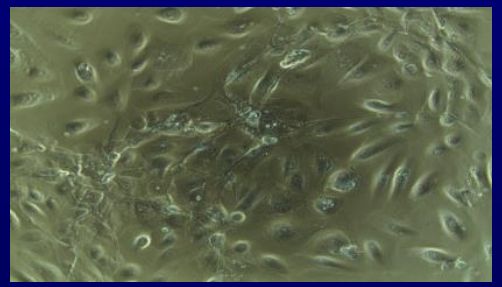


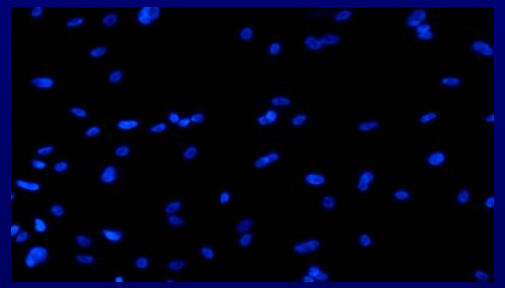
200 μM





400 μM



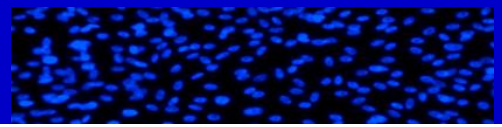


methotrexate inhibits proliferation of cultured PVR cells

phase contrast

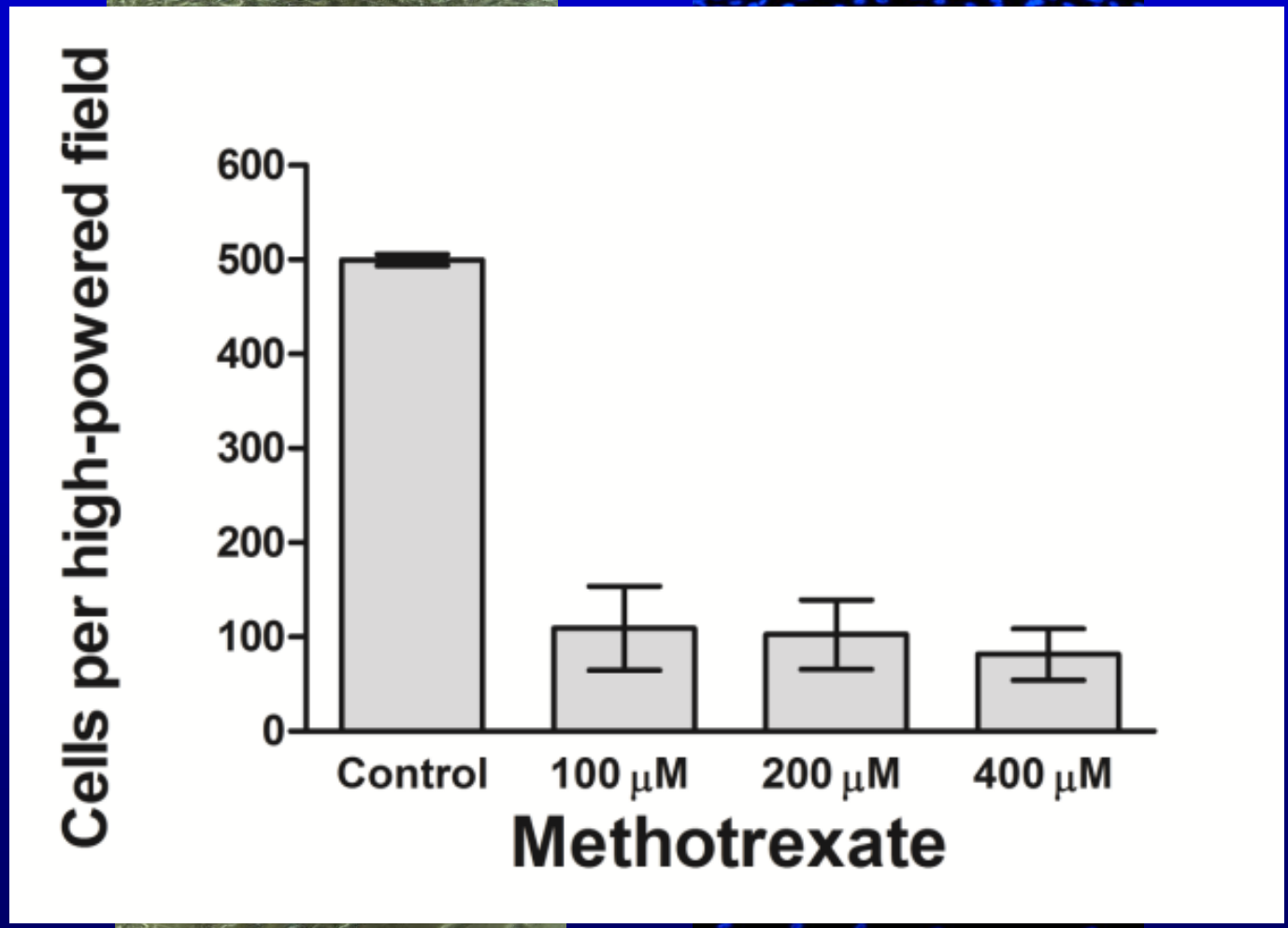
immunofluorescence

control

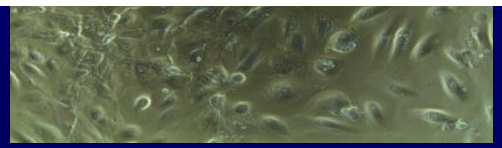


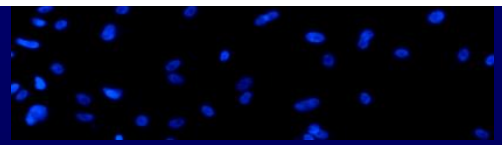
100 μM

200 μM



400 μM



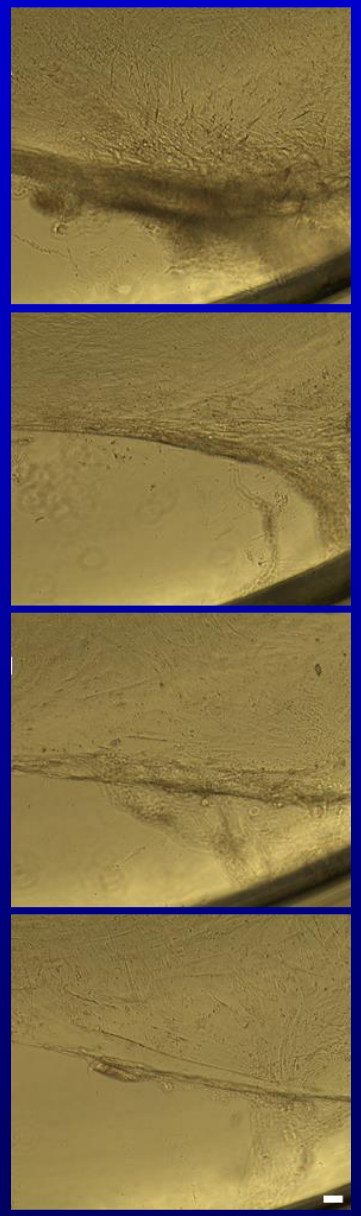


control

100 μM

200 μM

400 μM

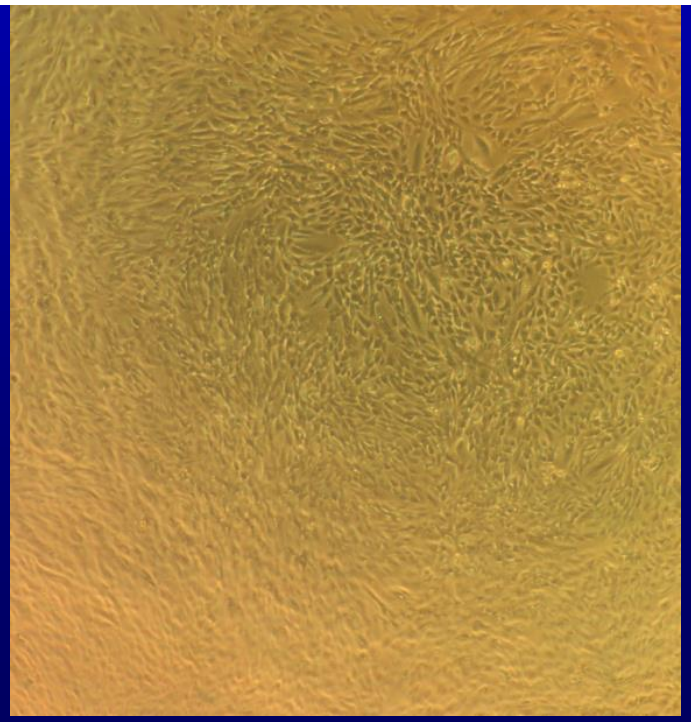


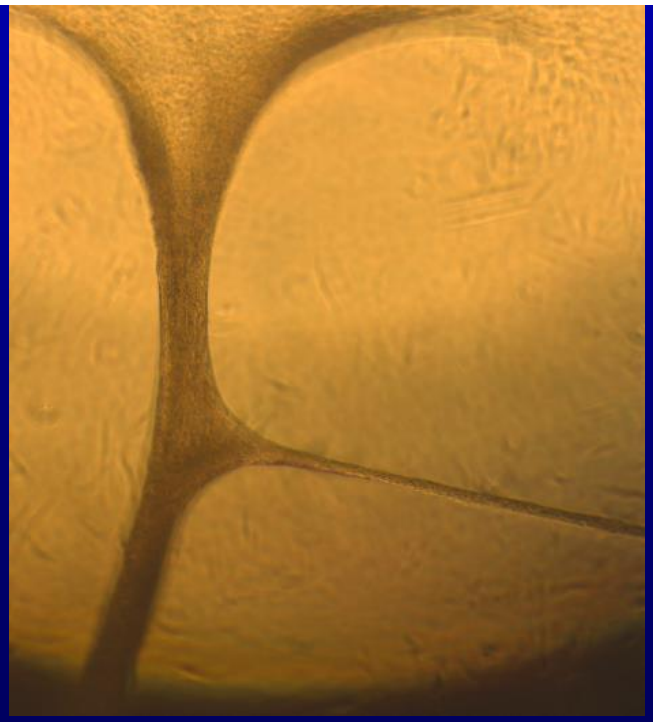
methotrexate inhibits band formation in cultured PVR cells

Lab Studies

Effect of Methotrexate on an In Vitro Patient-Derived Model of Proliferative Vitreoretinopathy

Dhanesh Amarnani,[1] Arturo Israel Machuca-Parra,[1] Lindsay L. Wong,[1] Christina K. Marko,[1] James A. Stefater,[2] Tomasz P. Stryjewski,[2] Dean Eliott,[2] Joseph F. Arboleda-Velasquez,[1] and Leo A. Kim[1,2]





Helio Vision Co-Founders

Josef von Rickenbach

- Founder, Chairman, and former CEO of PAREXEL, one of the world's leading biopharmaceutical services providers
- PAREXEL has been involved in the development of 94% of the top 200 best-selling drugs in the world

Tomasz Stryjewski

- Chief Resident and Director of the Eye Trauma Service at Mass. Eye and Ear
- Ophthalmology residency at Mass. Eye and Ear/ Harvard Medical School; Internal medicine at Mass. General Hospital; MD (honors) from Harvard Medical School

16 Additional Eyes

- 8 recurrent retinal detachment / PVR
- 8 open globe injuries

16 Additional Eyes

- 8 recurrent retinal detachment / PVR
- 8 open globe injuries
  - 13 injections / patient

16 Additional Eyes

- 8 recurrent retinal detachment / PVR
- 8 open globe injuries
  - 13 injections / patient

  - >95% compliance

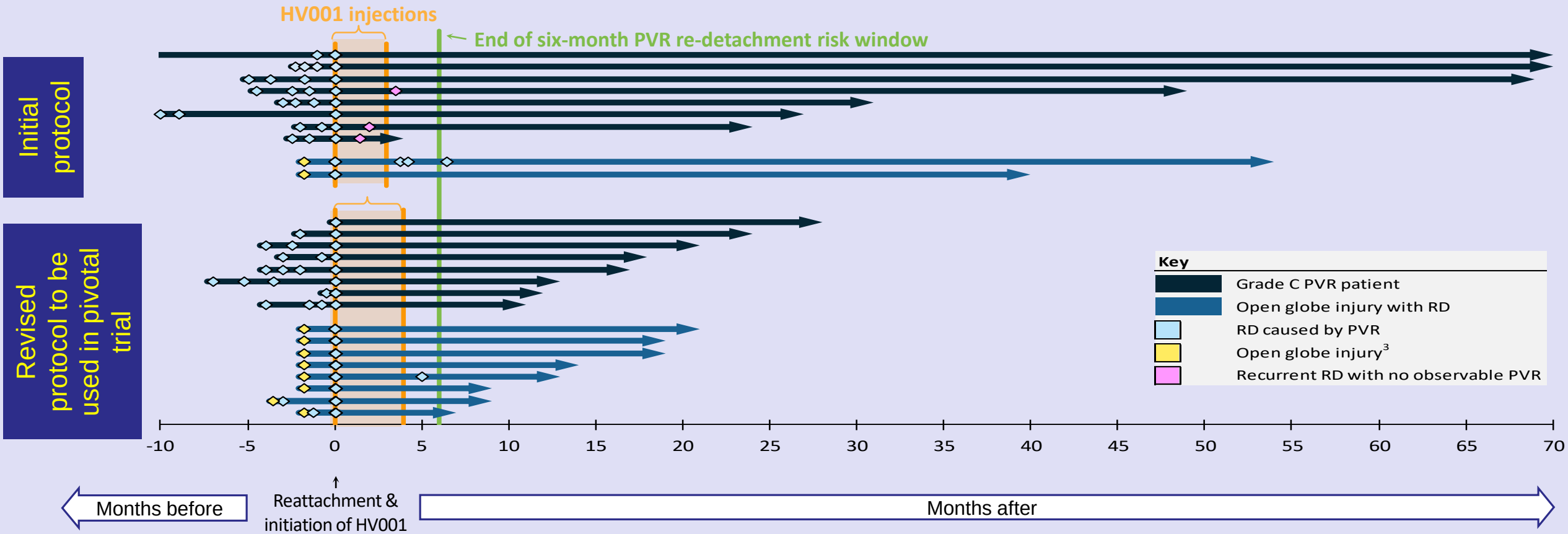
16 Additional Eyes

- 8 recurrent retinal detachment / PVR
- 8 open globe injuries

  - 13 injections / patient

    - 1 developed retinal detachment / PVR
    - 2 developed hypotony
    - 3 eyes minimal epiretinal membranes

Strong Human Efficacy Data



10 Initial Eyes +16 Additional Eyes

Percent of patients with at least one re-detachment due to any cause							
	Grade C PVR		Open globe injury		All patients		
HV001							
Initial protocol	38%	(3/8)	50%	(1/2)	40%	(4/10)	
Revised protocol	0%	(0/8)	13%	(1/8)	6%	(1/16)	(Protocol to be used in pivotal trial)
Combined	19%	(3/16)	20%	(2/10)	19%	(5/26)	
Standard of care[1,2]	54%		47%		51%		

Planned Phase III Trial Design

	Control Arm 100 Subjects	Intervention Arm 100 subjects	
	Routine Surgical Care Plars Plana Vitrectomy	**Routine Surgical Care** Plars Plana Vitrectomy	**Experimental Care** Injection #1: Intraoperatively Methotrexate 400mcg/0.1ml
Operative Day 0			
Post-Op Day 1	Routine Post-Op Visit VA, IOP, Photo, & OCT	Routine Post-Op Visit VA, IOP, Photo, & OCT	
Post-Op week 1	Routine Post-Op Visit VA, IOP, Photo, & OCT	Routine Post-Op Visit VA, IOP, Photo, & OCT	Injection #2: Methotrexate 400mcg/0.1ml
Post-Op week 2			Injection #3: Methotrexate 400mcg/0.1ml
Post-Op week 3			Injection #4: Methotrexate 400mcg/0.1ml
Post-Op week 4	Routine Post-Op Visit VA, IOP, Photo, & OCT	Routine Post-Op Visit VA, IOP, Photo, & OCT	Injection #5: Methotrexate 400mcg/0.1ml
Post-Op week 5			Injection #6: Methotrexate 400mcg/0.1ml
Post-Op week 6			Injection #7: Methotrexate 400mcg/0.1ml
Post-Op week 7			Injection #8: Methotrexate 400mcg/0.1ml
Post-Op week 8	Routine Post-Op Visit VA, IOP, Photo, & OCT	Routine Post-Op Visit VA, IOP, Photo, & OCT	Injection #9: Methotrexate 400mcg/0.1ml
Post-Op week 10			Injection #10: Methotrexate 400mcg/0.1ml
Post-Op week 12	Routine Post-Op Visit VA, IOP, Photo, & OCT	Routine Post-Op Visit VA, IOP, Photo, & OCT	Injection #11: Methotrexate 400mcg/0.1ml
Post-Op week 14			Injection #12: Methotrexate 400mcg/0.1ml
Post-Op week 16	Routine Post-Op Visit VA, IOP, dilated exam	Routine Post-Op Visit VA, IOP, dilated exam	Injection #13: Methotrexate 400mcg/0.1ml
Post-Op Month 6	Routine Post-Op Visit VA, IOP, dilated exam	Routine Post-Op Visit VA, IOP, dilated exam	

Contingent on funding, regulatory review, and other factors.

Summary

- Methotrexate a promising candidate to study for the prevention of PVR
  - antiproliferative
  - antiinflammatory
- Repeat injections match disease time-course
- Safety and efficacy demonstrated in Phase 1b study in humans & additional eyes

ALDEYRA THERAPEUTICS™

Ocular Disease Area Program Updates

- Proliferative Vitreoretinopathy
- Dry Eye Disease
- Allergic Conjunctivitis
- Upcoming Milestones

Nasdaq: ALDX

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ALDEYRA THERAPEUTICS™

Ocular Disease Area Program Updates

- Proliferative Vitreoretinopathy
- Dry Eye Disease
- Allergic Conjunctivitis
- Upcoming Milestones

Nasdaq: ALDX

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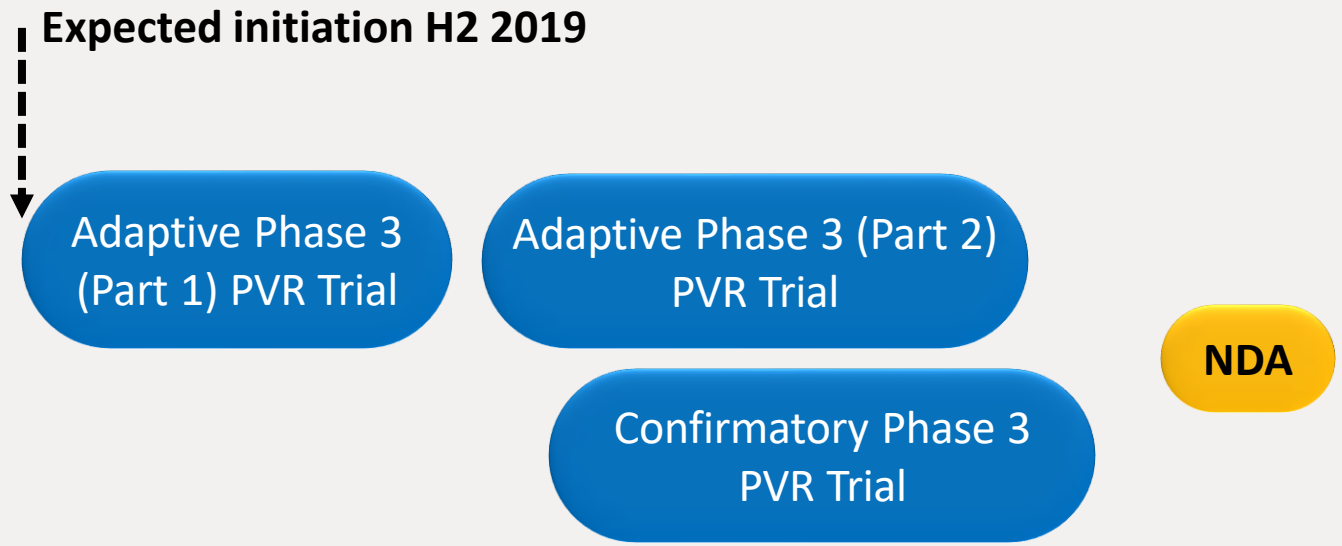
ADX-2191: Adaptive Phase 3 Proliferative Vitreoretinopathy Clinical Program Expected to Initiate H2 2019

Adaptive Phase 3 Program

- Part 1 controlled, randomized trial design
- Confirm endpoints, safety and tolerability
- Confirm sample size for subsequent trial

Phase 3 Program Design Elements



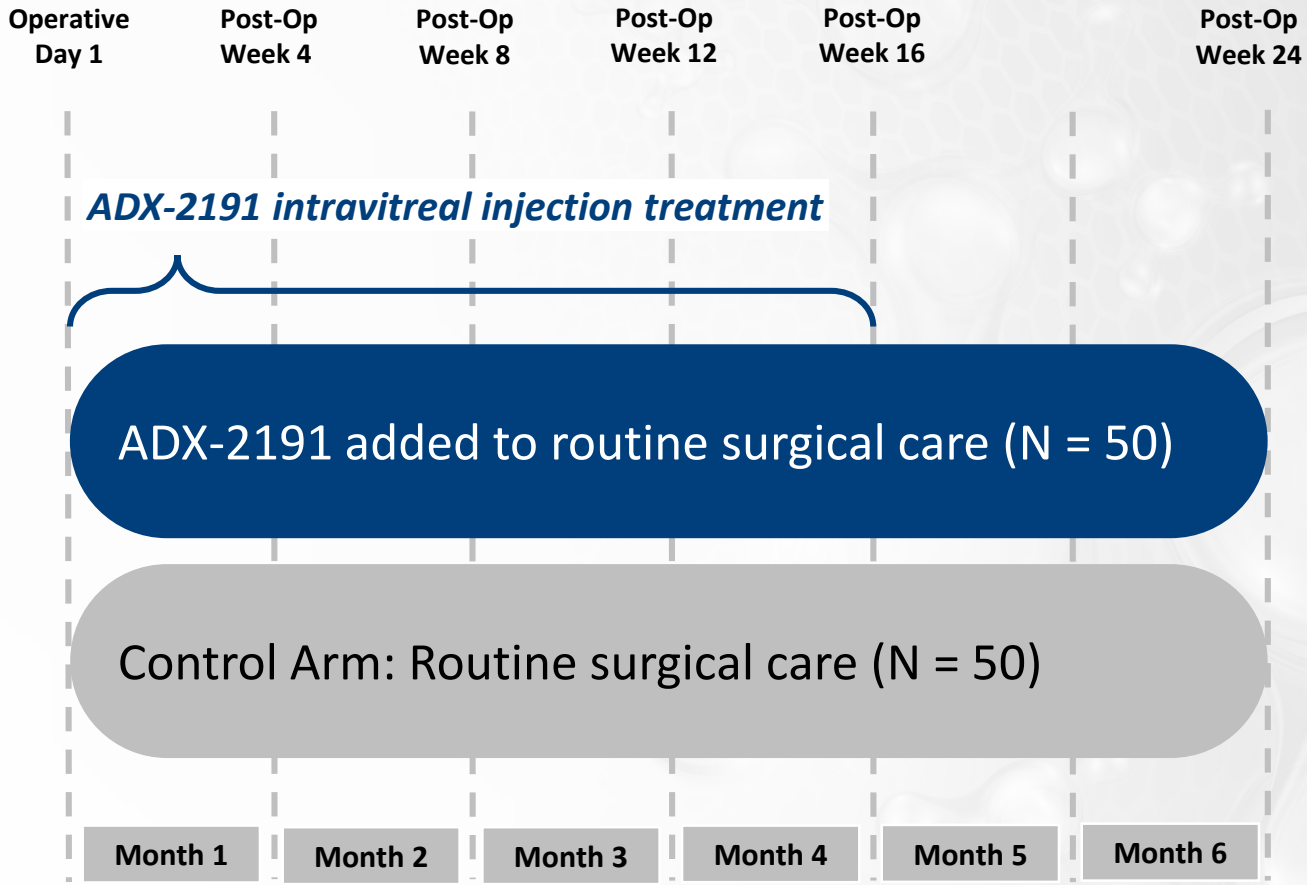
Illustrative only

PVR = Proliferative vitreoretinopathy

ADX-2191: Adaptive Phase 3 (Part 1) Proliferative Vitreoretinopathy Clinical Trial Design

- **Primary objective:**
  - Evaluate efficacy of intravitreal ADX-2191 injections for prevention of recurrent retinal detachment due to proliferative vitreoretinopathy (PVR)
- **Design:**
  - Multi-center, non-masked, randomized, controlled, two-part, adaptive Phase 3 clinical trial
- **Inclusion highlights:**
  - Recurrent retinal detachment due to PVR, or
  - Retinal detachment associated with open-globe trauma
- **Dosing regimen:**
  - At surgery, weekly (x8), and then every other week (x4) intravitreal ADX-2191 injections
- **Endpoint:**
  - Retinal re-detachments due to PVR requiring re-operation within 6 months:
    1. OCT demonstrating fovea-off retinal detachment
    2. Photographic documentation retinal detachment

Adaptive Phase 3 PVR Clinical Trial Design: Part 1



OCT = Optical Coherence Tomography

ALDEYRA THERAPEUTICS™

Ocular Disease Area Program Updates

- Proliferative Vitreoretinopathy
- Dry Eye Disease
- Allergic Conjunctivitis
- Upcoming Milestones

Nasdaq: ALDX

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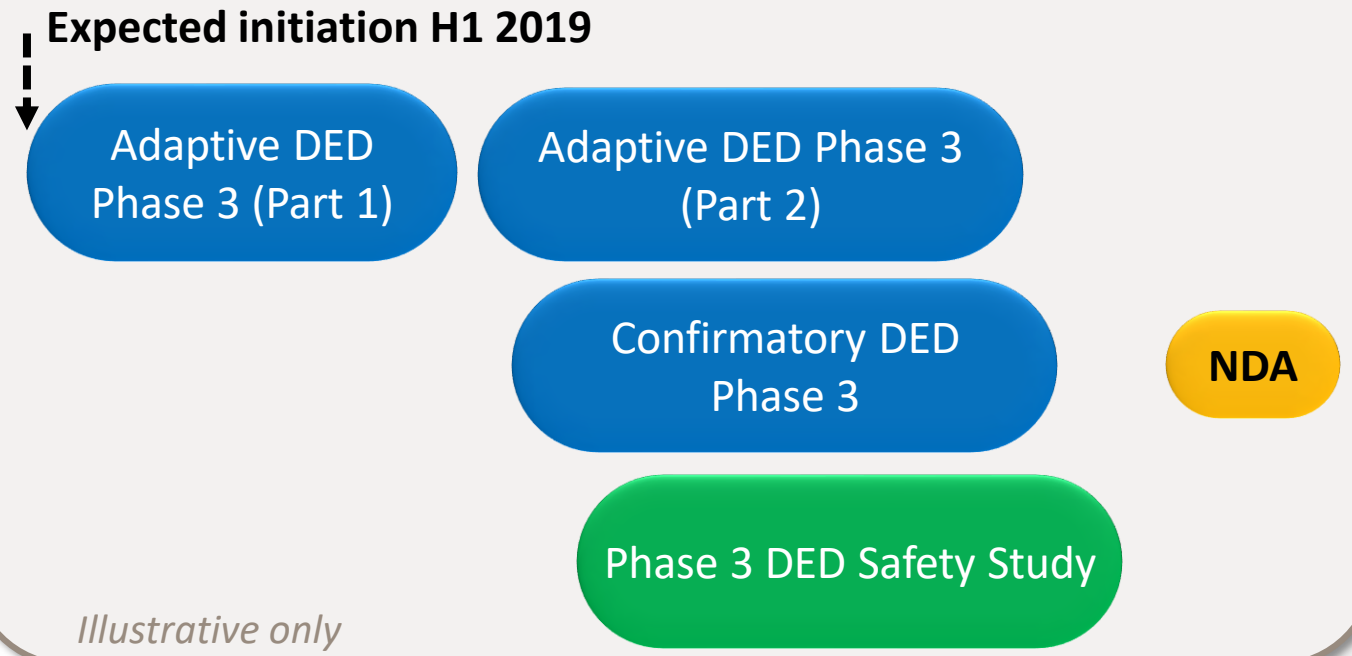
Reproxalap: Adaptive Phase 3 Dry Eye Disease Clinical Program Expected to Initiate H1 2019

Adaptive Phase 3 Program

- Confirm symptom and sign endpoints from Phase 2b trial
- Confirm dosing regimen (QID vs. QID to BID taper)
- Confirm sample size for subsequent trial

Phase 3 Program Design Elements



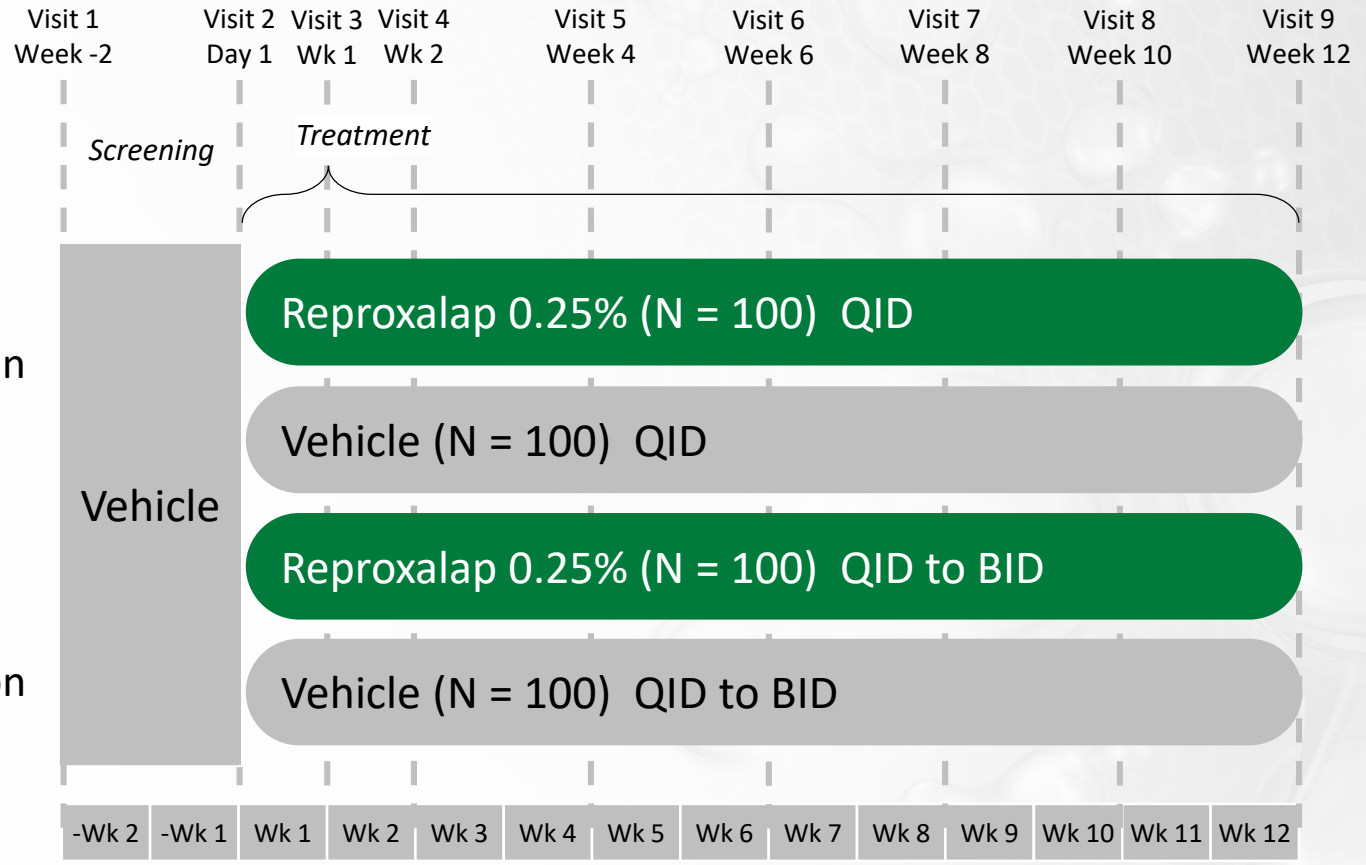
Adaptive design, co-primary endpoints and innovative analysis strategy confirmed with FDA at EOP2 Meeting

DED = Dry eye disease
BID = Two times daily
QID = Four times daily
EOP2 = End of Phase 2

Reproxalap:
Adaptive Phase 3 (Part 1) Dry Eye Disease Clinical Trial Design

- **Primary objective:**
  - Evaluate efficacy of reproxalap ophthalmic solution (0.25%) vs. vehicle to confirm dosing regimen and sample size for Part 2
- **Inclusion/exclusion criteria:**
  - Same as used for Phase 2b
  - Moderate to severe dry eye disease
- **Co-primary endpoints:**
  - Ocular dryness score (0-100mm VAS) and fluorescein nasal region staining
- **Analysis strategy:**
  - Both co-primary endpoints will be assessed using Mixed Model Repeated Measures (MMRM) from week 2 to week 12
  - Both co-primary endpoints will be assessed based on separate pre-specified patient populations
    - Ocular dryness score (OD4SS): baseline score of $\geq$ 3
    - Fluorescein nasal staining: baseline score $\geq$ 2

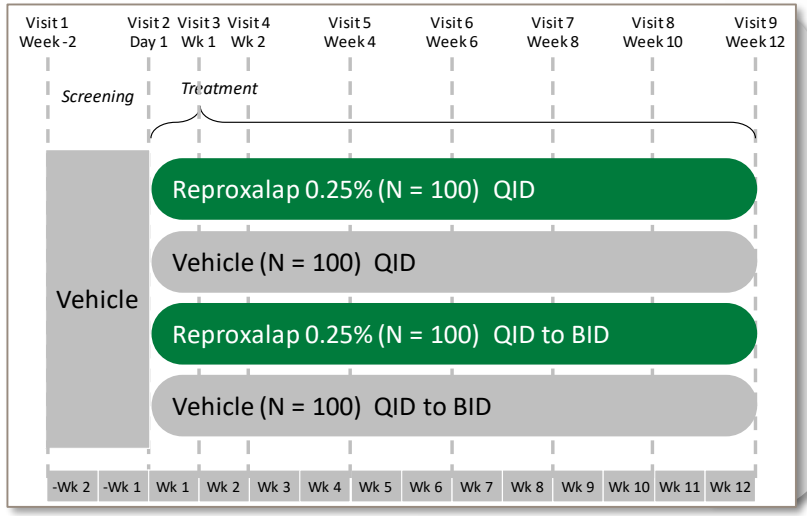
Phase 3 Dry Eye Disease Clinical Trial: Part 1



VAS = Visual analog scale
OD4SS = Ocular Discomfort 4-Symptom Score

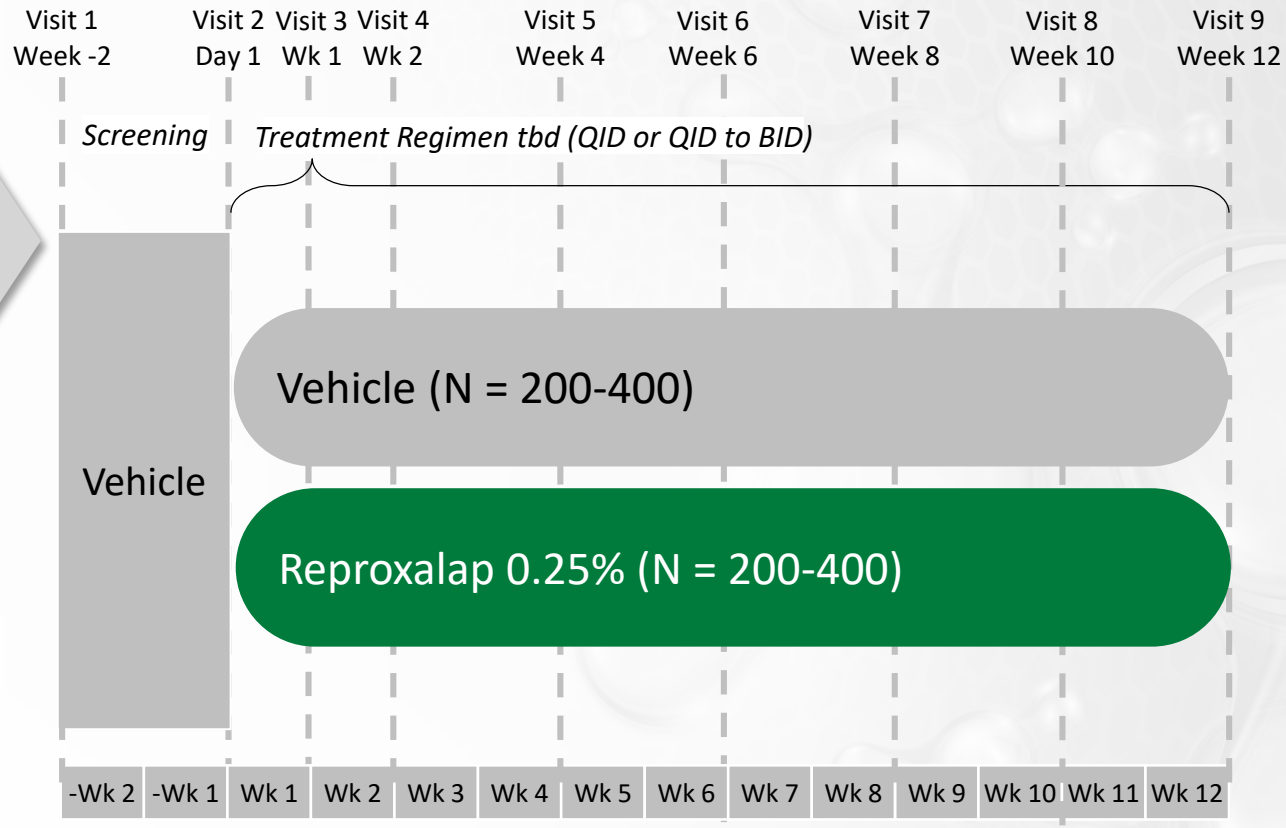
Reproxalap:
Adaptive Phase 3 (Part 2) Dry Eye Disease Clinical Trial Design

Phase 3 Dry Eye Disease Clinical Trial: Part 1



✓ Confirmed sample size
✓ Confirmed dosing regimen

Phase 3 Dry Eye Disease Clinical Trial: Part 2



Phase 3 Dry Eye Disease Clinical Trial: Part 2

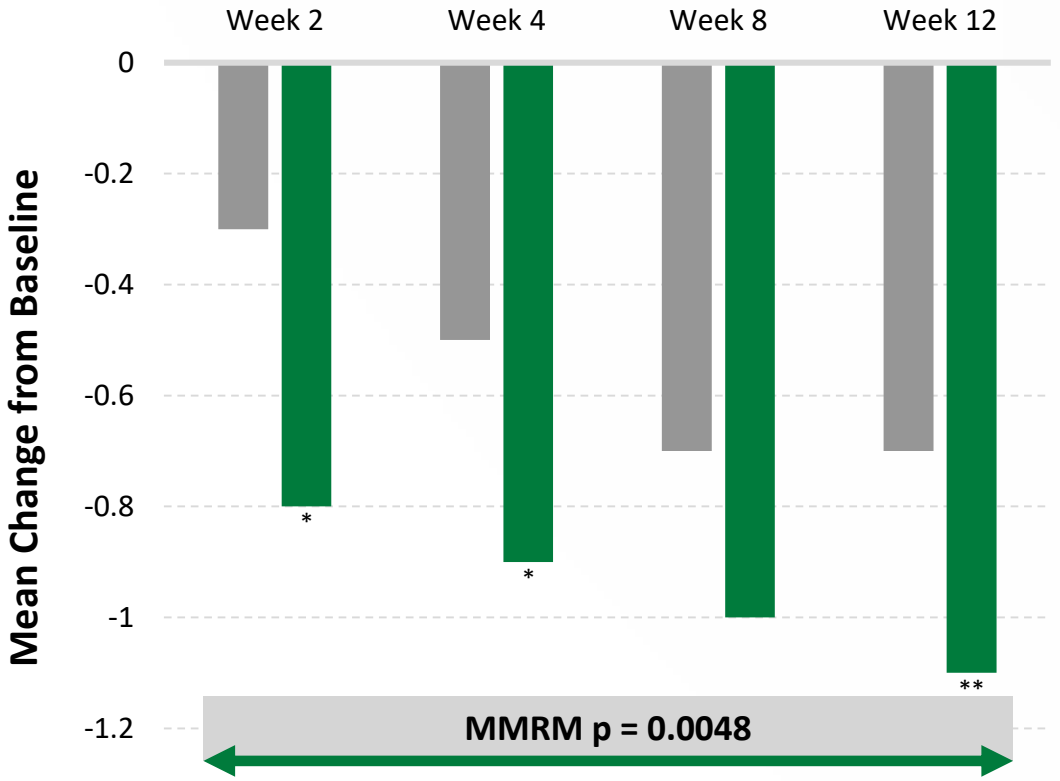
- **Primary objective:**
  Evaluate efficacy of reproxalap ophthalmic solution (0.25%) vs. vehicle on co-primary symptom and sign endpoints
- **Population selection and design:**
  Same as Part 1

Reproxalap: Dry Eye Disease Symptom and Sign Endpoints Achieved in Phase 2b Clinical Trial

Primary Symptom Endpoint for Phase 3 DED

OD & 4-Symptom Questionnaire: Dryness (0-5)

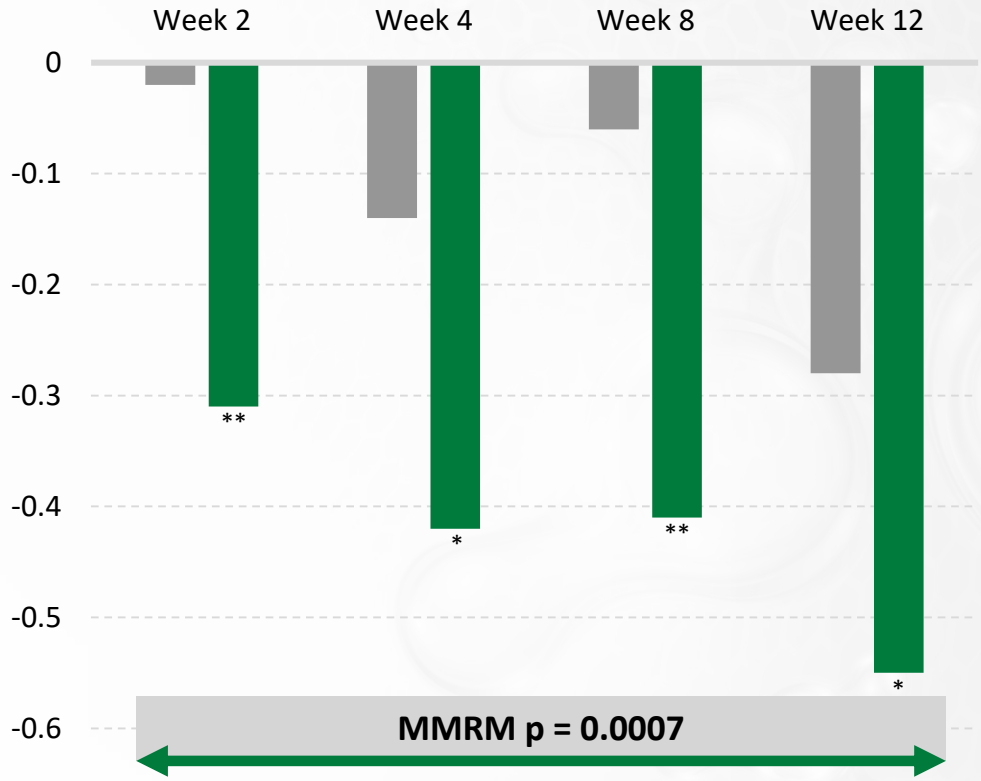
Baseline Score ≥ 3 (N=69|69)



Primary Sign Endpoint for Phase 3 DED

Fluorescein Staining: Nasal (0-4)

Baseline Score ≥ 2 (N=62|56)



Vehicle Reproxalap (0.25%)

p values subject to change based on quality control analysis

Source: Reproxalap DED Phase 2b clinical trial results

*p<0.05 **p<0.01

OD = Ocular Discomfort

MMRM = Mixed effect Model Repeated Measures

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Ocular Disease Area Program Updates

- Proliferative Vitreoretinopathy
- Dry Eye Disease
- Allergic Conjunctivitis
- Upcoming Milestones

Nasdaq: ALDX

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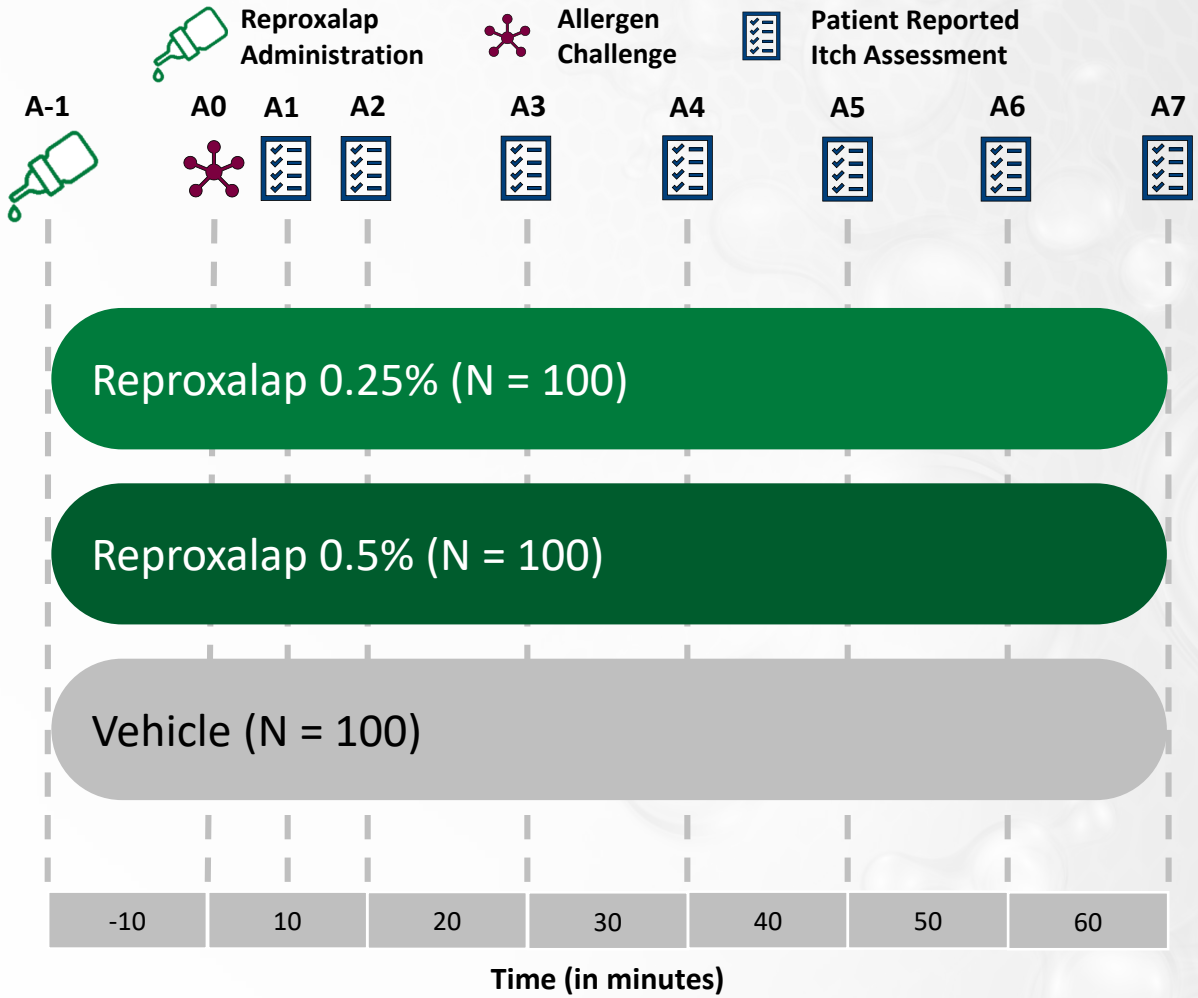
Reproxalap:
ALLEVIATE Phase 3 Trial Design in Allergic Conjunctivitis

- **Primary objective:**
  - Evaluate efficacy of reproxalap ophthalmic solutions (0.25% & 0.5%) compared to vehicle for the treatment of ocular itching associated with acute allergic conjunctivitis
- **Inclusion/exclusion highlights:**
  - Positive history of ocular allergies and positive skin test reaction to a seasonal allergen
  - Positive bilateral conjunctival allergen challenge (CAC) reaction of ≥2.5 for itching and ≥2 for redness within 10 min of allergen instillation at first baseline visit
  - Positive bilateral CAC reaction for at least two out of first three time points following challenge at second baseline visit
- **Endpoints:**
  - Ocular itch score area under the curve (primary)
  - Two-point responder comparison (key secondary)
- **Results expected to be announced early 2019**

ALLEVIATE is the first of two required Phase 3 clinical trials, pending regulatory review. In preparation for a subsequent Phase 3 clinical trial, Aldeyra is conducting clinical method development studies to assess the feasibility of measuring ocular itching following environmental exposure to allergen.

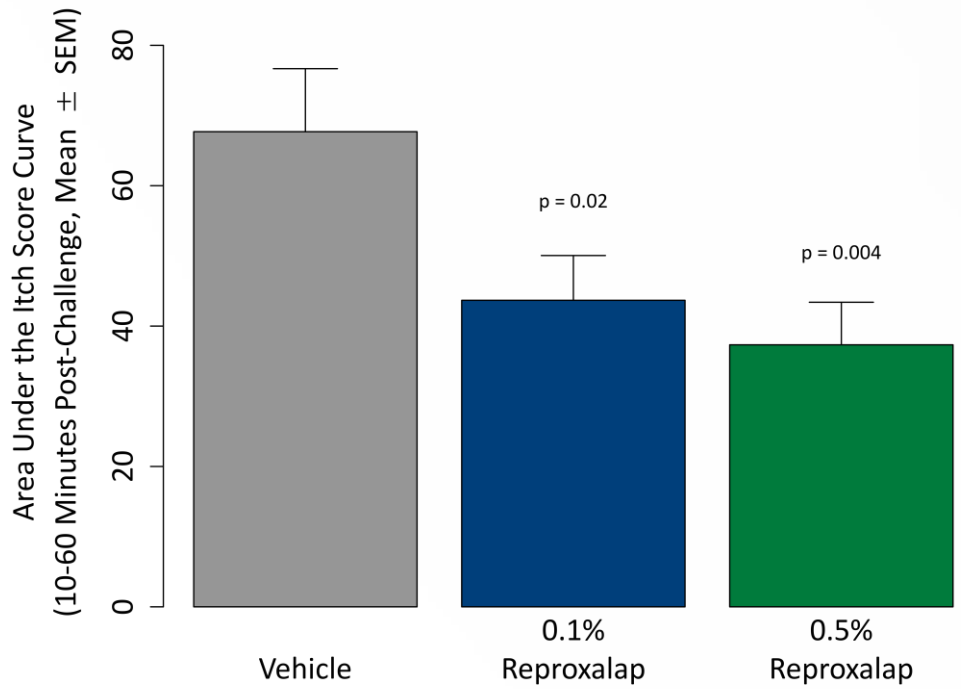
Phase 3 Conjunctival Allergen Challenge Trial



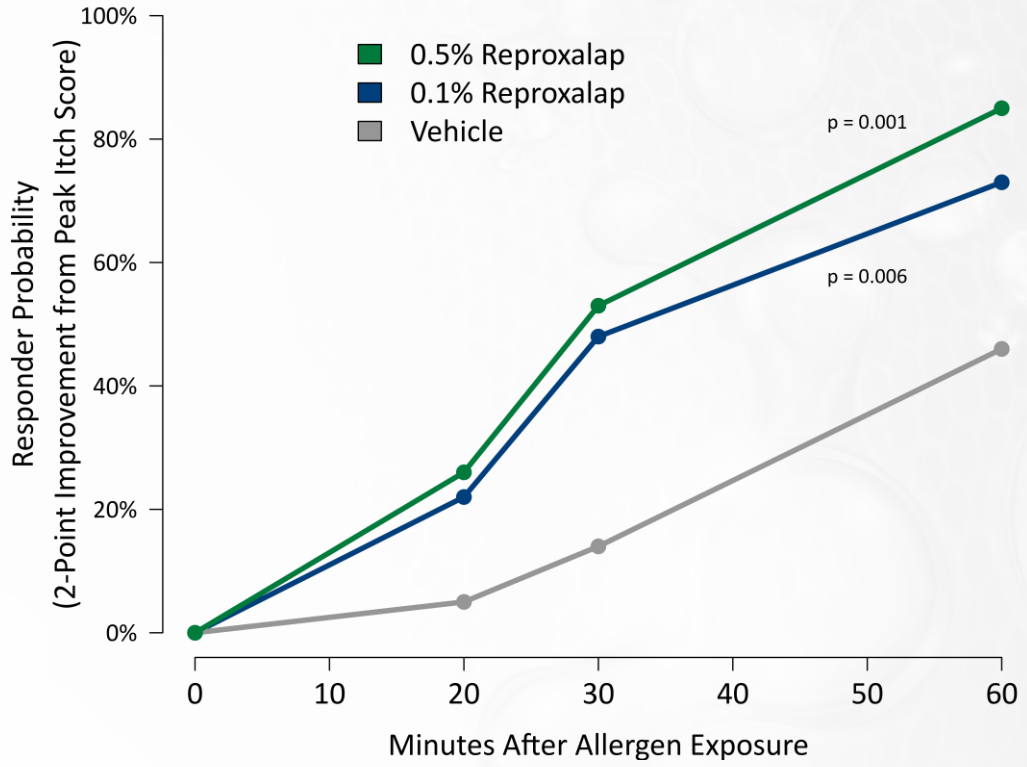
Further information can be found on www.clinicaltrials.gov: Trial #NCT03494504.

Reproxalap: AC Ocular Itch Area Under The Curve and Responder Endpoints Achieved in Phase 2b Clinical Trial

Area Under the Curve: Ocular Itch Score (0-4)



Probability of Response: Ocular Itch Score (0-4)



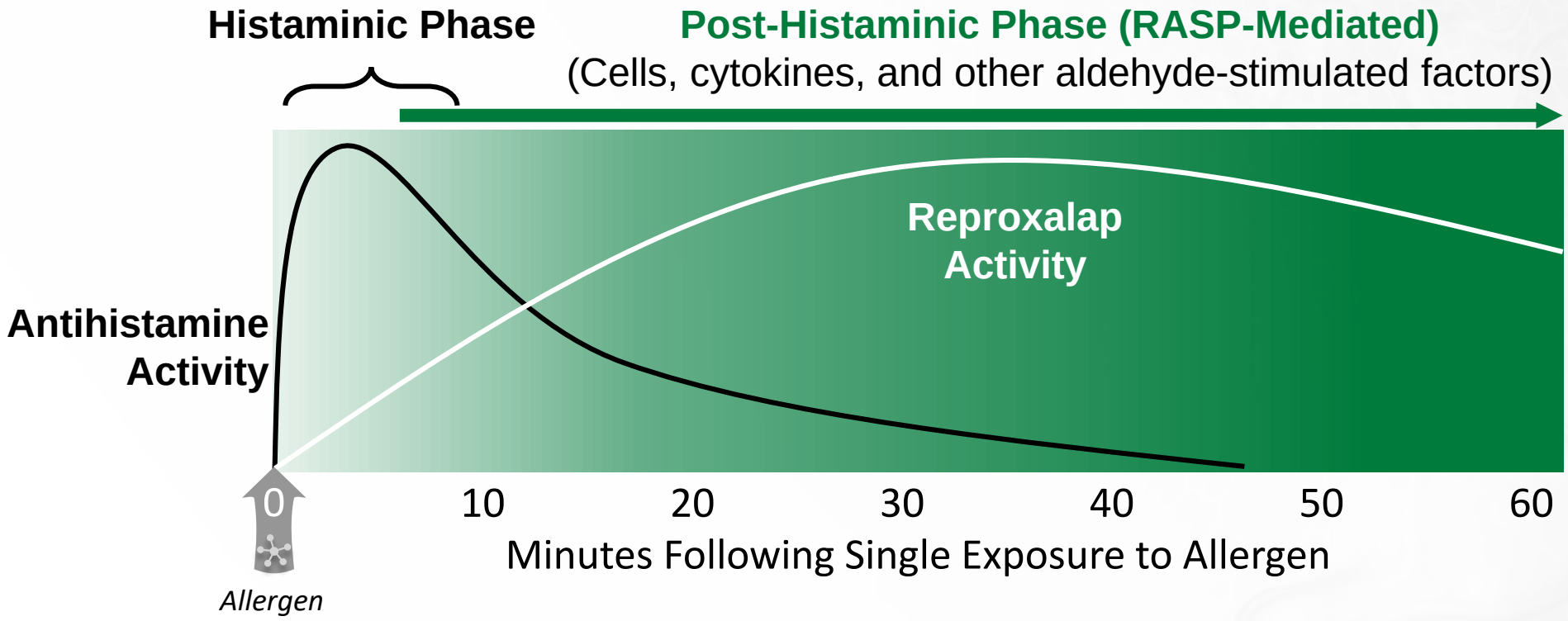
Improvement in itch score over one hour after allergen exposure statistically greater for reproxalap vs. vehicle

Clinically significant response rate of reproxalap statistically higher than that of vehicle

Source: Reproxalap AC Phase 2b clinical trial results (~30 patients per arm, seasonal allergy)

AC = Allergic conjunctivitis

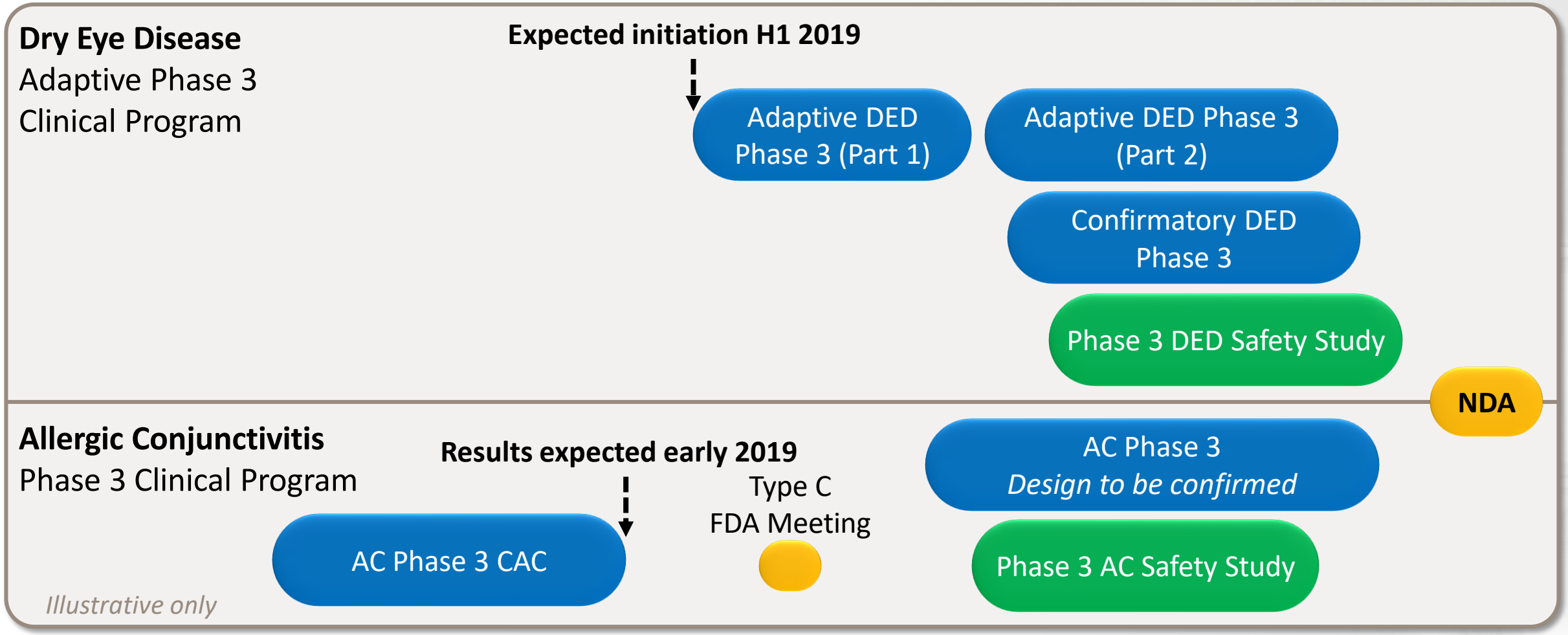
Reproxalap's Novel Mechanism of Action has the Potential to Provide More Durable Activity Than Antihistamines



Reproxalap has the potential to be uniquely effective in post-histaminic allergy, for which no drug is approved, and which affects all allergic conjunctivitis patients.

RASP = Reactive Aldehyde Species

Reproxalap: Parallel Dry Eye Disease and Allergic Conjunctivitis Phase 3 Clinical Programs Support Concurrent NDA Filings



DED = Dry eye disease
AC = Allergic conjunctivitis

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Ocular Disease Area Program Updates

- Proliferative Vitreoretinopathy
- Dry Eye Disease
- Allergic Conjunctivitis
- Upcoming Milestones

Nasdaq: ALDX

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Multiple Upcoming Ocular Disease Area Clinical Program Milestones

Ocular Disease Area Anticipated Milestones*

2019

2020

Results — **Early 2019**: Reproxalap ALLEVIATE Phase 3 allergic conjunctivitis trial

Initiate — **H1 2019**: Reproxalap Phase 3 dry eye disease clinical trial program

Results — **H2 2019**: Reproxalap SOLACE Phase 3 noninfectious anterior uveitis trial

Initiate — **H2 2019:** ADX-2191 Phase 3 proliferative vitreoretinopathy clinical trial program

Initiate — **2020:** ADX-103 Phase 1/2 retinal disease clinical trial

*Contingent on funding, regulatory review, and other factors.

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Ocular Disease Area Market Opportunities

- Proliferative Vitreoretinopathy
- Dry Eye Disease and Allergic Conjunctivitis
- Noninfectious Anterior Uveitis
- Pathway to Commercialization

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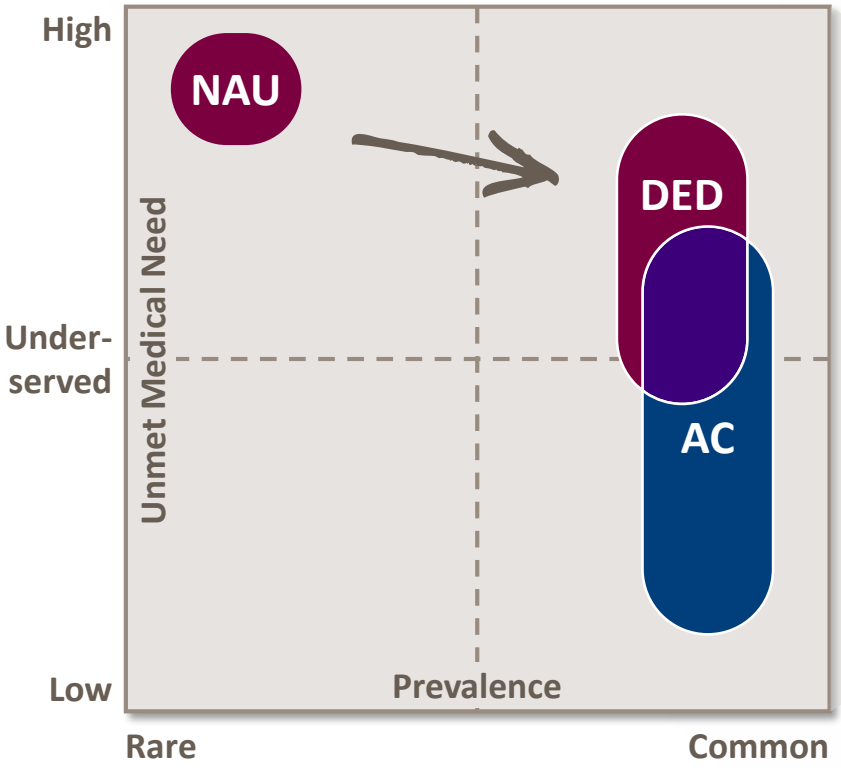
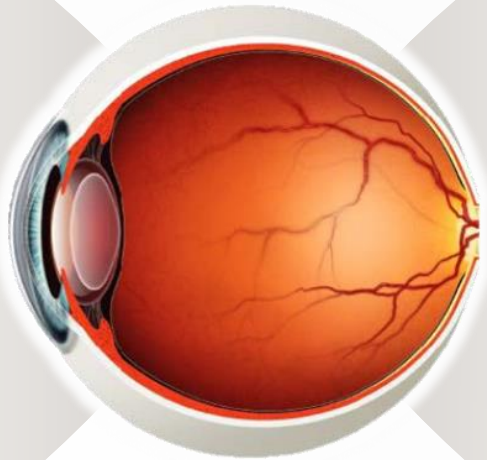
We Intend to Target Unmet Medical Needs in Anterior and Posterior Ocular Diseases

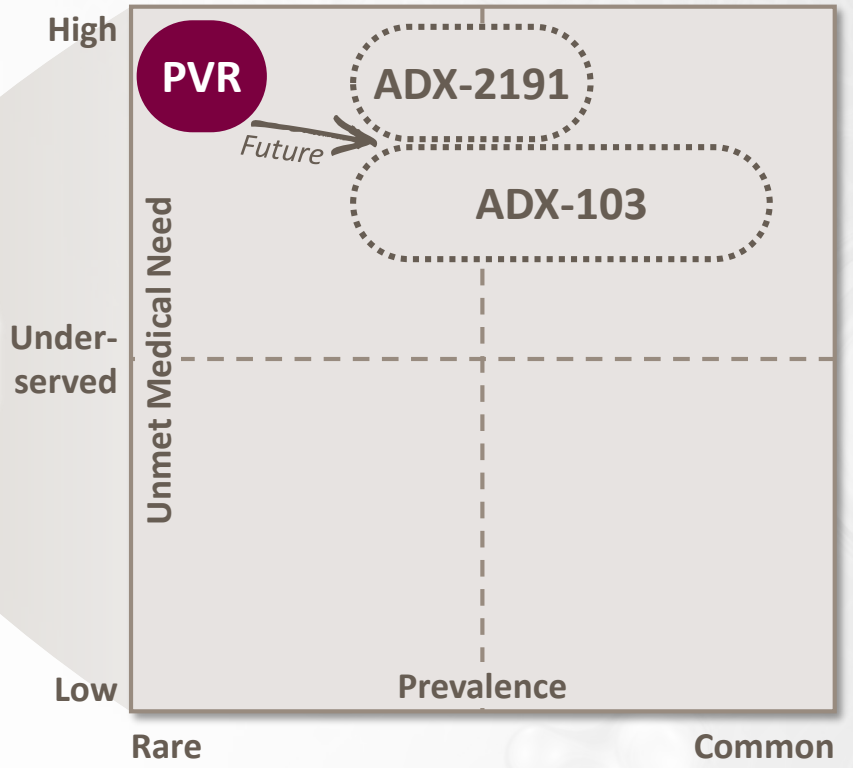
Anterior Opportunities



- ✓ Clear unmet and underserved medical need
- ✓ Novel treatment solutions
- ✓ Label expansion potential



Posterior Opportunities



NAU = Noninfectious anterior uveitis
DED = Dry eye disease
AC = Allergic conjunctivitis
PVR = Proliferative vitreoretinopathy

ALDEYRA THERAPEUTICS™

Ocular Disease Area Market Opportunities

- Proliferative Vitreoretinopathy
- Dry Eye Disease and Allergic Conjunctivitis
- Noninfectious Anterior Uveitis
- Pathway to Commercialization

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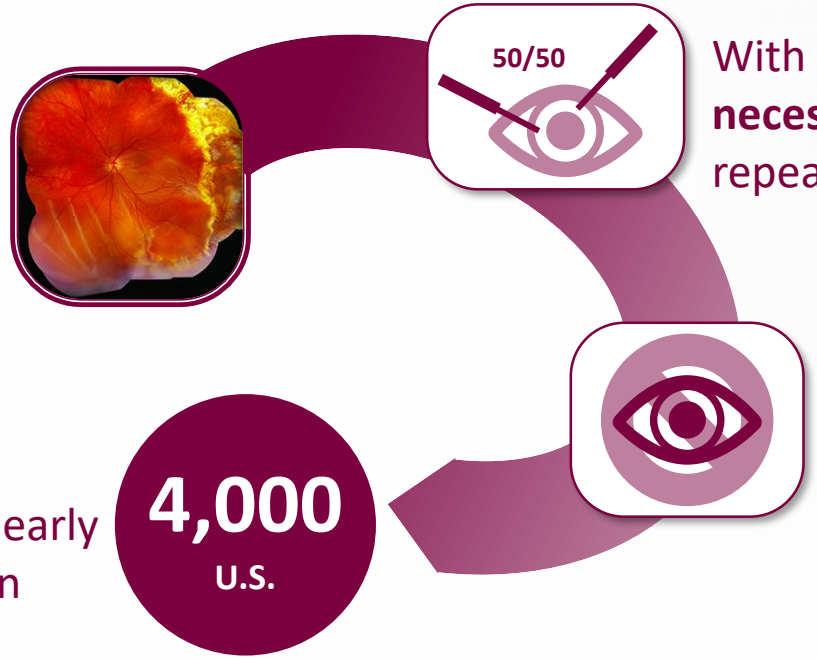
PVR: A Rare Sight-Threatening Retinal Disease

PVR is the **leading complication** of retinal detachment surgery and **prevents successful reattachment**



With no therapies available, PVR **necessitates repeat surgery** with a repeat surgery **failure rate of ~50%**

PVR is an **serious condition leading to permanent vision loss** in up to 75% of cases

PVR is a **rare disease**, with ~4,000 patients per year in the U.S. and nearly twice as many in Europe and Japan

Source: Aldeyra internal estimates based on primary and secondary market research; published literature

PVR = Proliferative vitreoretinopathy

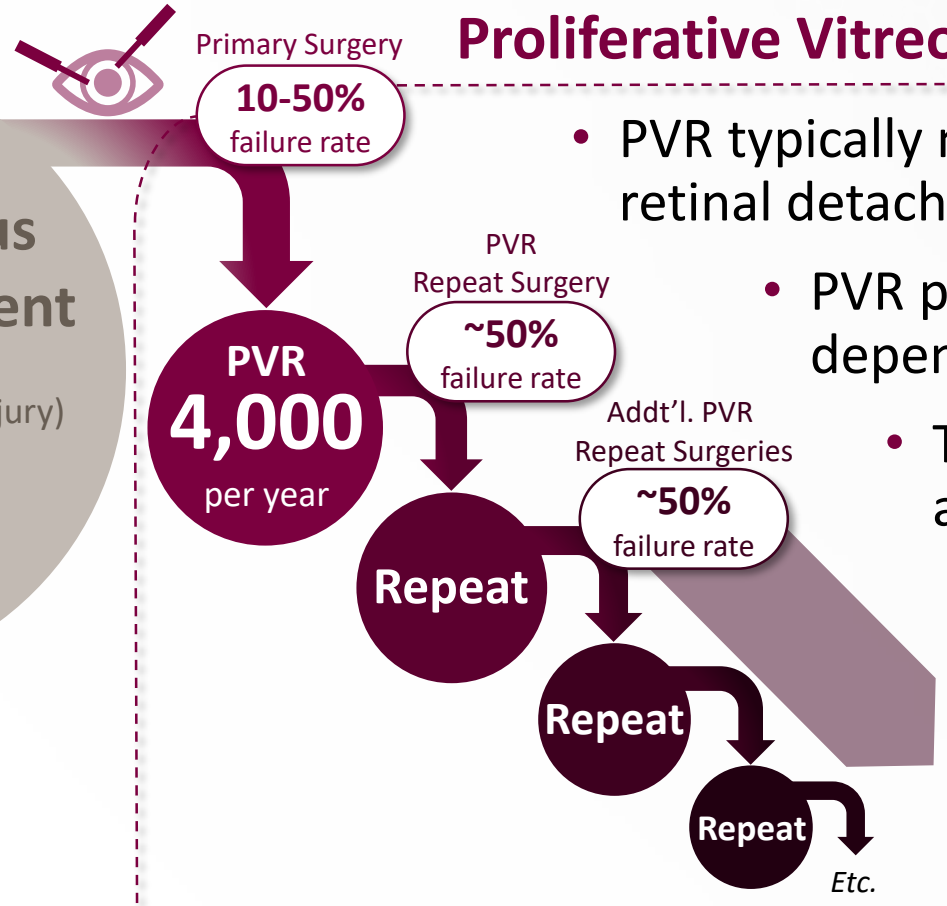
PVR: High Unmet Medical Need With No Approved Therapies

U.S. Estimates

Rhegmatogenous Retinal Detachment

- Non-traumatic
- Traumatic (open-globe injury)

>28,000
per year



Proliferative Vitreoretinopathy

- PVR typically manifests 1-2 months after primary retinal detachment surgery
- PVR primary surgery failure rates vary depending on detachment etiology
- Today, PVR patients undergo 3-to-4 additional surgeries on average
- Vision and quality of life decreases with each procedure
- No FDA-approved therapy

Novel Approaches Needed

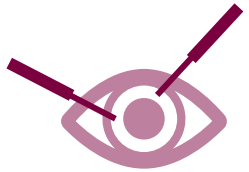
Source: Aldeyra internal estimates based on primary and secondary market research; published literature

ADX-2191: A Unique Approach and Novel Product Candidate for PVR

PVR: A Sight-Threatening Disease

Left untreated, retinal detachment due to **PVR can progress to permanent blindness**

No FDA- or EMA-approved therapy



Repeat surgery and subsequent **vision loss** currently the only possible course of action

A Unique Opportunity

ADX-2191

- A **novel approach and potential therapeutic breakthrough** in PVR treatment
- **Granted U.S. orphan designation**
- **Tolerability and reattachment success** during study period **demonstrated in Phase 1b** clinical trial
- Adaptive Phase 3 clinical trial **expected to initiate H2 2019**

PVR = Proliferative vitreoretinopathy

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Ocular Disease Area Market Opportunities

- Proliferative Vitreoretinopathy
- Dry Eye Disease and Allergic Conjunctivitis
- Noninfectious Anterior Uveitis
- Pathway to Commercialization

Nasdaq: ALDX

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DED and AC:
Persistently Disturbing and Overlapping Disease Burdens

Dry Eye Disease

20 million or more **adults in the U.S.** suffer from DED

DED **increases with age**, with those over age 50 three times more likely to suffer from DED

Women are twice as likely to suffer from DED than men

Significant **negative quality of life** impact

DED+AC Comorbidity

Studies have shown that **DED and AC can be interrelated** and often overlap

~50-60% of **DED and AC patients experience** clinically significant **itch and dryness**

Allergen exposure can contribute to **DED seasonality**

Significant **negative quality of life** impact **x2**

Allergic Conjunctivitis

Up to 30 million of **AC sufferers** in the U.S. **do not respond adequately** to or are **dissatisfied with antihistamines**

AC patients experience symptoms throughout **all decades of adult life**

AC can result in **acute, intermittent, and chronic** symptoms

Significant **negative quality of life** impact

Source: Aldeyra internal estimates based on primary and secondary market research; published literature

DED = Dry eye disease
AC = Allergic conjunctivitis

DED and AC: Chronic Diseases With Inadequate Therapies

Dry Eye Disease

Current Rx options **may take up to six weeks or longer** to achieve even modest efficacy

Up to 75%

Up to 75% of patients with DED **are not satisfied with current prescription options**

Up to 50%

Up to 50% of patients **treated for DED** with current therapies **fail and discontinue**

Underserved Patient Population

DED+AC Comorbidity

DED, AC or both?

Differential diagnosis is difficult and treating both conditions together is complex

Current Rx **DED treatments are not effective against AC** and vice versa

Antihistamine use can cause and exacerbate **eye dryness**

Unmet Medical Need

Allergic Conjunctivitis

Many AC **patients make significant sacrifices** due to lack of drug activity

24%

Antihistamines are not effective in an estimated 24% of treated AC patients

2%

~2% of AC patients have severe symptoms and **may be corticosteroid-dependent**

Underserved Patient Population

Source: Aldeyra internal estimates based on primary and secondary market research; published literature

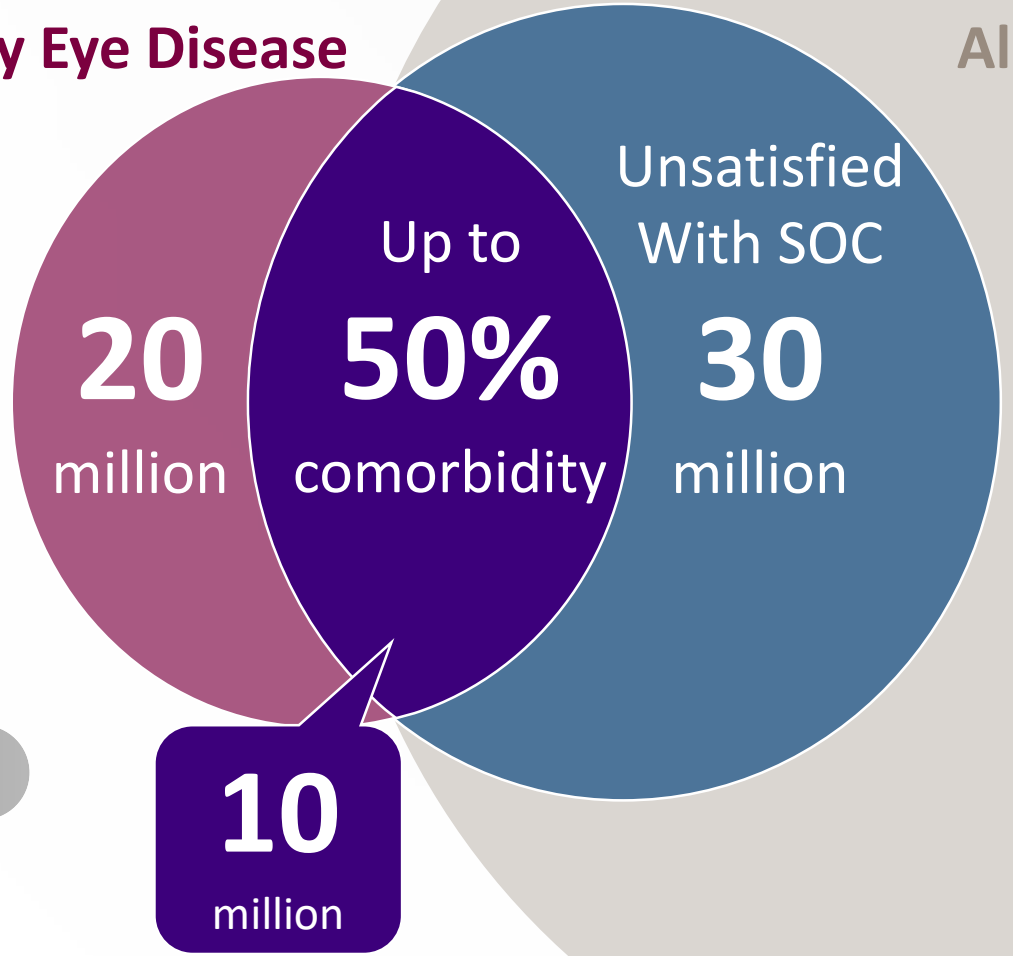
DED = Dry eye disease
AC = Allergic conjunctivitis

DED and AC:
Large Market Opportunities With Unmet Medical Needs

U.S. Patient Estimates

- Significant negative quality of life
- Complex, overlapping, and difficult to treat chronic conditions
- Substantial unmet medical need with current treatments

Novel Approaches Needed



Source: Aldeyra internal estimates based on primary and secondary market research; published literature

DED = Dry eye disease
AC = Allergic conjunctivitis
SOC = Standard of Care

Reproxalap: A Unique and Novel Product Candidate for DED and AC

Dry Eye Disease	DED+AC Overlap	Allergic Conjunctivitis
Reproxalap in DED	**Reproxalap**	**Reproxalap in AC**
Early and consistent symptom and sign improvements in Phase 2b clinical trial	**Observed improvements in both DED and AC** Phase 2b clinical trials	**Clinically significant and durable symptom response** in Phase 2b clinical trial
Broad symptom and sign improvements in Phase 2b clinical trial	Both **patients and physicians** have a **strong desire for better** DED and AC **treatments**	**Effective in post-histaminic allergy**, for which no drug is approved

Novel mechanism of action and differentiated approach **to treat DED and AC**

DED = Dry eye disease
AC = Allergic conjunctivitis

ALDEYRA THERAPEUTICS™

Ocular Disease Area Market Opportunities

- Proliferative Vitreoretinopathy
- Dry Eye Disease and Allergic Conjunctivitis
- Noninfectious Anterior Uveitis
- Pathway to Commercialization

Nasdaq: ALDX

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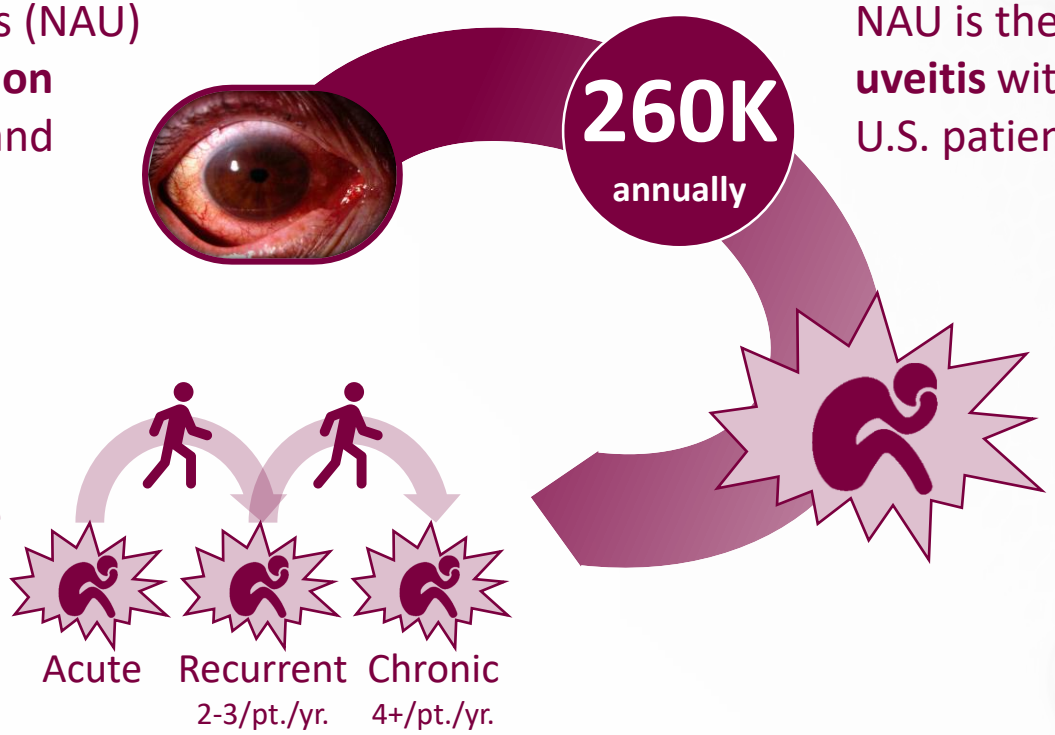
NAU: A Severe Ocular Inflammatory Disease

Disease Burden Overview

Noninfectious anterior uveitis (NAU) is a **severe ocular inflammation** causing **pain**, **photophobia**, and **vision loss**



NAU is the **most common form of uveitis** with an estimated 260,000 U.S. patients per year

~50% of NAU patients have **recurrent or chronic conditions** requiring multiple interventions per year

NAU **dramatically impacts quality of life**, leading to loss of work and significant economic burden

Source: Aldeyra internal estimates based on primary and secondary market research; published literature

NAU: Significant Repeat Episodes and Steroid Toxicity Creates the Need for Novel Approaches

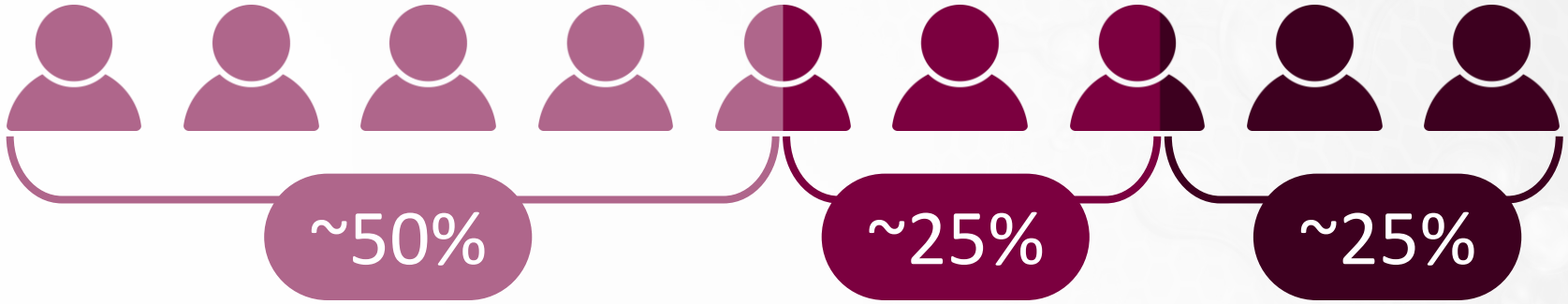
U.S. Estimates

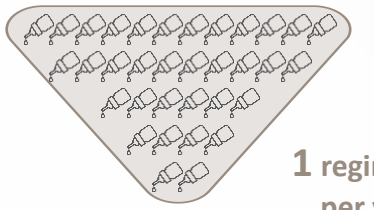
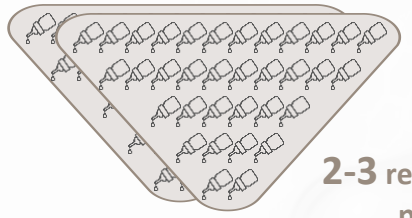
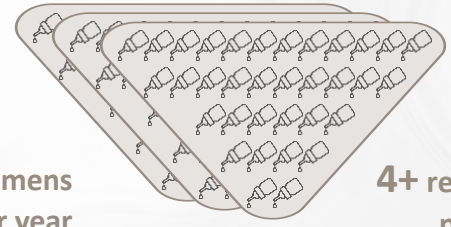
Prevalence:
Approximately 260,000 noninfectious anterior uveitis (NAU) patients in the U.S.

Corticosteroid treatment:
8-12 times/day tapered over 4-6 weeks

Prolonged corticosteroid usage increases risks of serious side effects

NAU episode frequency:



	Acute	Recurrent	Chronic
	Single flare within a year	*Relapse 3-12 months after initial episode*	*Relapse <3 months after initial episode*
Steroid use:	 1 regimen per year	 2-3 regimens per year	 4+ regimens per year
Safety risk:	 *4-6 weeks of treatment*	 *8-12+ weeks of treatment*	 *12-18+ wks. of treatment*

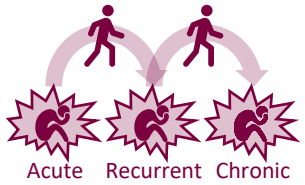
Potential corticosteroid side-effects include glaucoma, cataracts, corneal ulceration, ptosis, delayed wound healing, and ocular infection

Source: Aldeyra internal estimates based on primary and secondary market research; published literature

NAU = Noninfectious anterior uveitis

Reproxalap: A Unique and Novel Product Candidate for NAU

NAU: A Serious Inflammatory Disease With Inadequate Current Therapy



~50% of noninfectious anterior uveitis (NAU) patients have **recurrent or chronic conditions** requiring multiple interventions per year

Corticosteroids currently SOC and **require monitoring due to serious toxicities**

Prolonged usage may lead to **glaucoma**, **cataracts**, **corneal ulceration**, and other serious side effects

A Unique Opportunity

Reproxalap

- A **novel and differentiated** approach to treat NAU
- **Reduced anterior chamber cell count** observed in a Phase 2 clinical trial, **statistically non-inferior to corticosteroid treatment**
- **Safety and tolerability without IOP increase** in a Phase 2 clinical trial
- SOLACE Phase 3 clinical trial **results expected H2 2019**

NAU = Noninfectious anterior uveitis
SOC = Standard of Care
IOP = Intraocular pressure

Source: Aldeyra internal estimates based on primary and secondary market research; published literature

ALDEYRA THERAPEUTICS™

Ocular Disease Area Market Opportunities

- Proliferative Vitreoretinopathy
- Dry Eye Disease and Allergic Conjunctivitis
- Noninfectious Anterior Uveitis
- Pathway to Commercialization

Nasdaq: ALDX

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We Intend to Commercialize Directly and Through Partnerships

Late Stage Programs	Estimated U.S. Population*	U.S. Healthcare Providers	Competitive Value Proposition	Infrastructure Requirement
Ocular Diseases				
Dry Eye Disease	20 million DED Up to 10 million with DED & AC 30 million AC	~18,000 ophthalmologists and ~40,000 optometrists	Potential benefits over current therapies, which do not work well for many patients	Medium sized sales force for national reach
Allergic Conjunctivitis				
Noninfectious Anterior Uveitis	260,000	~200 U.S. uveitis sub-specialists	Effective non-steroid alternative	Small targeted sales force
Proliferative Vitreoretinopathy	4,000	Retina specialists at targeted centers	Orphan: First and only Rx treatment	Small specialized operation
Systemic Diseases				
Sjögren-Larsson Syndrome	1,000	Geneticists and ped. neurologists	Orphan: First and only Rx treatment	Small specialized operation

Commercial Planning

✓ *Launch readiness*

✓ *Maximize value*

- Characterize the business model
- Prepare for commercialization
- Develop partnership options

*Aldeyra estimates of the addressable market

Source: Aldeyra internal estimates based on primary and secondary market research; published literature

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Conclusion

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Expected Development Milestones: Novel Approaches to Address Immune-Mediated Disease

Ocular Diseases: Anticipated Milestones*

- Reproxalap allergic conjunctivitis ALLEVIATE Phase 3 trial **results early 2019**
- Update — Reproxalap dry eye disease **Phase 3 clinical trial program initiation H1 2019**
- Update — Reproxalap noninfectious anterior uveitis SOLACE Phase 3 clinical trial **results H2 2019**
- Update — ADX-2191 Proliferative Vitreoretinopathy **Phase 3 clinical program initiation H2 2019**
- Update — ADX-103 retinal disease **Phase 1/2 clinical trial initiation 2020**

Systemic Diseases: Anticipated Milestones*

- Update — Reproxalap Sjögren-Larsson Syndrome RESET Phase 3 - Part 1 clinical trial **results H2 2019**
- Update — ADX-629 **Phase 1 clinical trial initiation H2 2019** followed by NASH and/or IBD Phase 2a
- ADX-1612 post-transplant lymphoproliferative disorder **Phase 2 clinical trial initiation 2019**
- ADX-1612 mesothelioma **Phase 2 clinical trial initiation 2019**

*Contingent on funding, regulatory review, and other factors.